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Effects of Chronic Heat or Cold Exposure on Growth and Blood Pressure in Rats

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Abstract: We studied the effects of various environmental temperatures on growth and blood pressure in rats. Spontaneously hypertensive rats (SHR) and their mother strain, normotensive Wistar–Kyoto rats (WKY) were used as the experimental animal. Rats of the two strains, SHR and WKY of 1 month old were divided into three groups randomly and they were housed in three rooms, of which temperatures were controlled at a constant, 30°C (H-group), 22-24°C (N-group) and 10°C (C-group), respectively.

Effects of environmental temperature on body weight gain were studied. Growth retardation was observed in the H-group of both strains. Maximal body weight gains were higher and reduced more quickly in SHR compared to those in WKY. In both SHR and WKY, at approximately 4 months old, the ratio of the tail to body surface areas was in the order of H-group > N-group > C-group in both strains.

Systolic blood pressure (BP) was measured by the tail cuff method at approximately 4 months old. In WKY, BP in the C-group was significantly higher than that in H-group. In SHR, the BPs of the three groups were high compared to those in WKY groups, to which rats were exposed since 1 month old. And the BPs of C-group and H-group were significantly high compared to that in N-group.

These facts indicate that effects of environmental temperature, to which rats were exposed since 1 month old, on growth were similar in WKY and SHR, and that the effects of the environmental temperature on systemic BP are clear in normotensive WKY, whereas in SHR, genetic expression of the hypertensive phenotype is consistent at various environmental temperatures.

Key Words: *Environmental temperature, Wistar-Kyoto-rats (WKY), Spontaneously hypertensive rats (SHR), Growth*

INTRODUCTION

There are many studies on the effects of environmental stress on growth and physiological conditions. The effects of chronic exposure to various environmental temperatures on the physiological conditions in rats have been reported. Cold-induced hypertension in rats was reported by Fregly *et al.* (1989).

Global warming is increasing, mainly due to industrial activities. A high environmental temperature may have severe effects in various fields including human health.

This study investigated animal models to indicate the effect of increased environmental temperature on the health of humans and other species. Experimental animal models for genetic hypertension, spontaneously hypertensive rats (SHR) and the mother strain, normotensive Wistar-Kyoto rats (WKY) were introduced (Okamoto & Aoki, 1963). These SHR rats were known as a genetically hypertensive rats, the hypertension is consistently developed with aging. It is interesting whether a development of genetic hypertension is modified or not by the

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exposure to the various environmental temperatures. The effects of chronic exposure to various temperatures on growth and the development of hypertension were studied in WKY and SHR.

METHOD

Male WKY and SHR were introduced from the breeding company (Charles River, Japan). Rats of the two strains, SHR and WKY of 1 month old were divided into three groups randomly and they were housed in three rooms, of which temperatures were controlled at a constant, 30°C (H-group), 22-24°C (N-group) and 10°C (C-group), respectively.

In one plastic cage, 3 or 4 rats were kept with wood shavings under a 12/12-hour light-dark cycle (light on 7:00-19:00) with food (F-2, Funahashi, Japan) and water *ad libitum*. The body weights (BW) of rats were measured using a balance every week. The predicted growth curves were obtained by fitting values of BW to the logistic function ($Y=a/\{1+b \exp(-cX)\}$, where Y is predicted BW, X is months from birth. a, b and c are constant). From these fitting curves, mean weight gain per week was calculated. At approximately 4 months old, the systolic blood pressure (BP) of rats was measured by the tail cuff method (PE-300, NARCO, USA) after the general warming, which induced tail vasodilation. In order to evaluate the tail surface area by calculation, assuming that the cross section of any portion of the rat tail is an exact circle, the entire length of the tail, from the anus to the tip of the tail, and the diameter at every 3 cm of the tail were measured using a slide caliper. Calculated body surface area was obtained by the equation, $S = 8.62 \times BW^{0.67}$ (S: total surface area (cm^2), BW: body weight(g), Lyzak & Hunter, 1987).

Values were expressed as Mean±S.D.. Statistical significance of change in parameters was determined Kruskal-Wallis test (Stat View 5.0, SAS Institute Inc.).

RESULTS

Body weight and body weight gain

The mean body weights (BW) of the three groups in WKY and SHR were plotted against time (month) after birth in Fig. 1-A, B. One-group was composed of 5-10 rats. As shown in Fig. 1, growth curves of SHR were steeper in comparison with those of WKY. And in both strains, WKY and SHR, the growth curves of the H-groups were under than those of the N-group and the C-group. In WKY, mean BW at near 4 months (M) old was 343±28 g in the C-group (n=10; 3.9M), 338±9g in the N-group (n=5; 4.0M) and 319±8 g in the H-group (n=5; 4.0M). There were no significant differences among these values. In SHR, the mean value of BW at 4 months old was 335±25 g in the C-group (n=7: 4.0 M), 346±21 g in the N-group (n=8; 4.0 M) and 310±16 g in the H-group (n=8; 4.0 M). The value of the H-group was significantly lower than those of the N and C groups ($P < 0.05$).

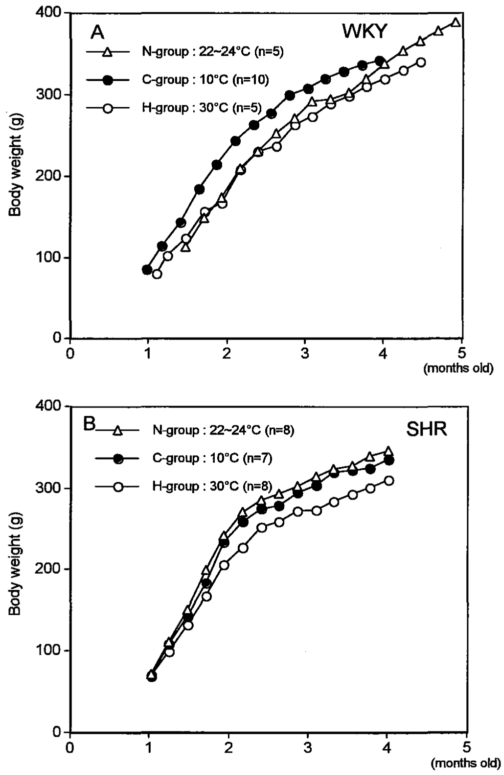

Fig. 1. Mean body weight of WKY (A) and SHR (B) exposed to the three different environmental temperatures, C-group (solid circles, WKY;n=10, SHR;n=7), N-group (open triangles, WKY;n=5, SHR;n=8), and H-group (open circles WKY;n=5, SHR;n=8).

Fitting curves of BW to the logistic equation in WKY are shown Fig.2-A. From these fitting curves, the mean weight gain per week was calculated (Fig. 2-B). In WKY, maximal values of weight gain are within the range of 1.5-2.5 months old. Maximal values of weight gain were 32.4 g/week in the C-group, 23.3 g/week in the N-group and 24.7 g/week in the H-group. Figure 3-A and B shows the fitting curves of BW and weight gain of SHR, respectively. In SHR, maximal values of weight gain are in the range of 1.5-2 months old, the value of weight gain at the peak was 39.7 g/week in the C-group, 42.3 g/week in the N-group, and 32.0 g/week in the H-group.

Curves of the weight gain in SHR were higher in the maximal zone, and thereafter those curves reduced more quickly than those of the WKY groups.

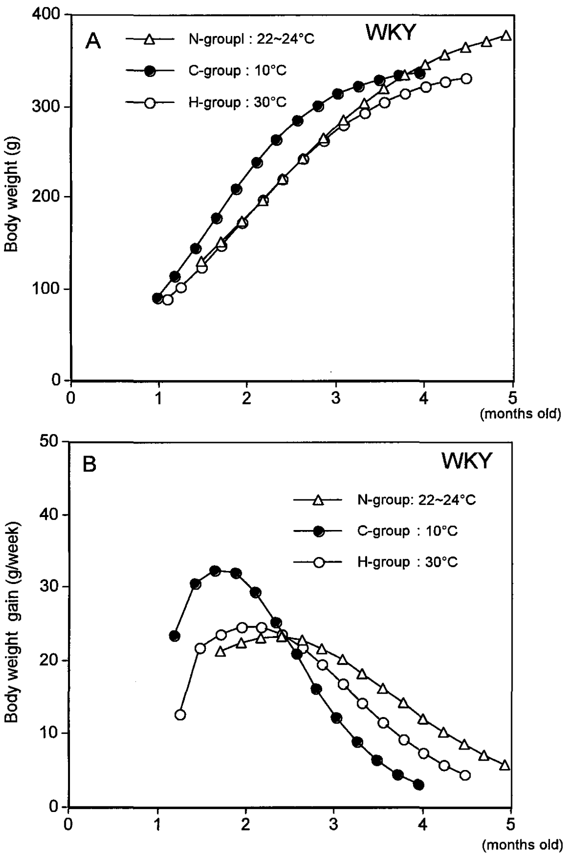

Fig. 2. Fitting curves of mean body weight to the logistic equation (A) and weight gains of the three rats groups of WKY (B).

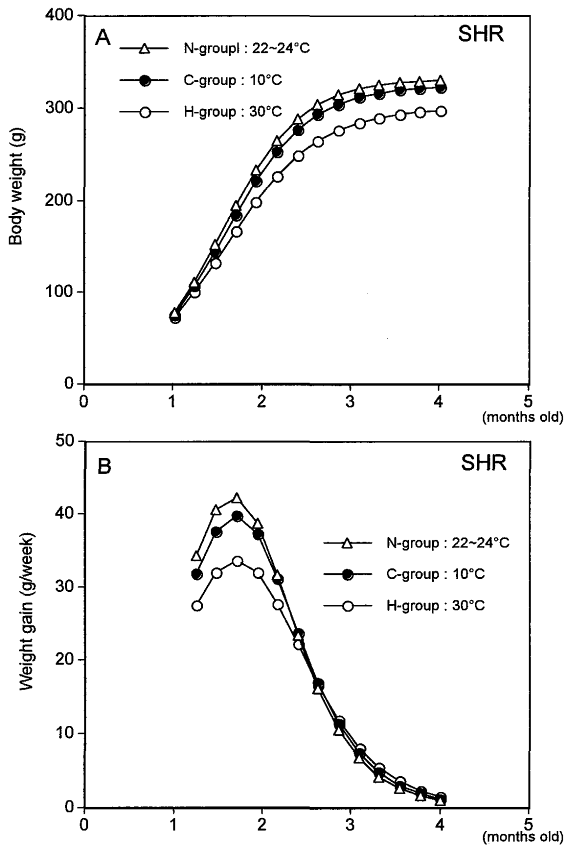

Fig. 3. Fitting curves of mean body weight to the logistic equation (A) and weight gains (B) of the three rats groups of SHR.

Tail growth

The body surface area of the rats was calculated by means of the equation, and the tail surface was also calculated by the diameter measured in each 3 cm of the tail from the anus to the tip of the tail.

In WKY, the ratio of the tail surface to the body surface area was 7.9 ±0.3 % in the C-group (n=10), 8.5±0.4% in the N-group (n=10), and 8.9±0.2% in the H-group (n=5), (Fig. 4-A). In SHR, the ratio was 7.0±0.1% in the C-group (n=7), 8.1±0.4 % in the N-group (n=8), and 9.0±0.3% in the H-group (n=8), (Fig. 4-B). In both strains, these values were significantly different ($P < 0.01$, or $P < 0.05$ only between N-group and H-group in WKY) from each other. Both in WKY and SHR, mean values of the ratio of the tail surface to the body surface areas were in the order of H-group > N-group > C- group.

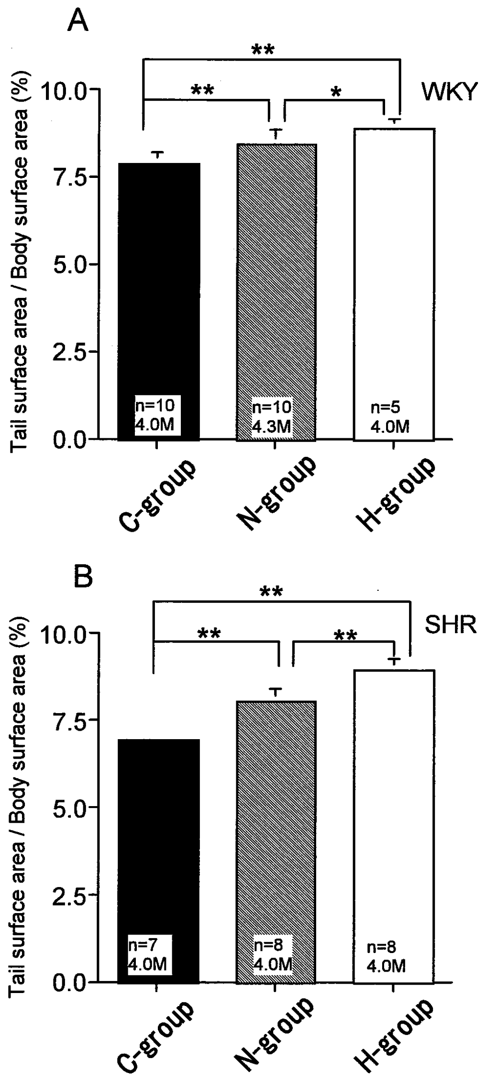

Fig. 4. Ratio of the tail surface area to body surface area in WKY (A) and SHR (B) at approximately 4 months old. Rats were chronically exposed to the three different environmental temperatures from 1 month old. Values are Mean ± SD, ** $P < 0.01$, * $P < 0.05$.

Systemic blood pressure

Systolic blood pressure (BP) was measured by the tail cuff method in rats of approximately 4 months old in both strains, which were reared exposed to the three different temperatures from 1 month old. In WKY, the BP was 134±8 mmHg in the C-group (n=6), 127±11 mmHg in the N-group (n=6) and 117±9 mmHg in the H-group (n=7). In WKY, the BP of the C-group was significantly ($P<0.05$) higher than that of the H-group (Fig. 5-A). In SHR, the BP was 179±12 mmHg in the C-group (n=7), 163±10 mmHg in the N-group (n=5) and 180 ±6 mmHg in the H-group (n=4) (Fig. 5-B). In the three groups of SHR, hypertension developed. Mean values of BP in both C-group and H-group were significantly ($P<0.05$) higher than that in the N-group.

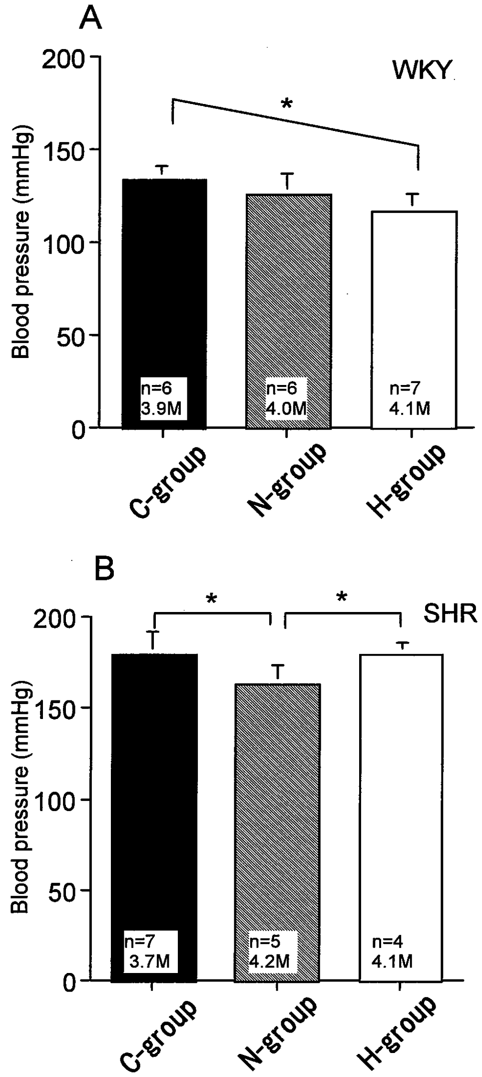

Fig. 5. Systolic blood pressure of WKY (A) and SHR (B) at approximately 4 months old. Rats were chronically exposed to the three different temperatures from 1 month old. Values are Mean ± SD, * $P < 0.05$.

DISCUSSION

Growth (Body weight)

Brobeck (1945) has already reported on body weight growth in albino rats, weight gain was greater at 86 °F (30°C) than 70°F (21.1°C) when food intake and activity were constant. On the other hand, it was reported that growth of the rat is prominent in the neutral temperature, and growth was retarded in the hot and cold environments (MacFarlane *et al.*,1959, Yamauchi *et al.*, 1981; Peeters *et al.*, 1989; Gordon 1990). In this study, both WKY and SHR, there was an inclination of growth retardation in chronic heat-exposure. Growth retardation of the hot environment was remarkable in the SHR (Fig. 1-A,B). These findings suggest that the growth of SHR is more susceptible to hot environmental stress than WKY.

Schork *et al.* (1994) studied the relationship between the growth and the development of hypertension in SHR, stroke-prone SHR (SHRSP) and WKY. They indicated that the growth is phasic and that there is a growth spurt peak at 50 days of age in each strain.

In this study, body weight gains (g/week) were calculated from the fitting curve of the experimental growth curve. In both WKY and SHR, maximal body weight gains were observed between 1.5 month and 2.5 months. The values of weight gain reduced more quickly in SHR compared to those in WKY. These results show the special features of body weight gain of SHR, and support the findings of Shork *et al.* (1994).

Growth (tail)

The effect of chronic exposure to various ambient temperatures on rat tail growth has been studied by Thorington (1966). Rat tails are short in a cold environment, whereas those are long in a hot environment. In this study, in both WKY and SHR, the ratio of the tail surface to body surface areas were significantly different depending on the exposed temperatures. These ratios were in the order of H-group > N-group > C-group. These results suggest that the effects of environmental temperatures were similar on the growth of rat tails in both WKY and SHR.

Growth and Hypertension

In this study, SHR and WKY were used as experimental animals, and the effect of chronic exposure on growth and development of hypertension were investigated. Schork *et al.* (1994) studied the relationship between growth and the development of hypertension in SHR, stroke-prone SHR (SHRSP) and WKY. They indicate that the time of maxiaml weight gain corresponds to the onset of a blood pressure spurt. These results support the idea that growth and rising blood pressure are intimately linked. In this study, the peak value of weight gain of C-group was the highest among the three groups of WKY. And the peak values of weight gain of three groups of SHR were higher than those of the corresponding groups in WKY. It is interesting fact that development of hypertension was definite in C-group of WKY and in the three groups of SHR, in which four groups the high peak values of weight gain were observed.

Reasons for cold-induced hypertension

In this study, mild hypertension was shown in cold-exposed WKY as reported by Feregly *et al.* (1989). The BP of the H-group of WKY was lower than that of the control, N-group. This suggests that chronic heat-exposure might have a reverse effect of the cold exposure on such a system in normotensive WKY.

During chronic exposure to cold, it was reported that ß-adrenergic responsiveness increased in the cardiovascular system, both in the heart and the blood vessels in the tail skin in the rat (Barney *et al.*, 1980). And plasma noradrenaline concentration increased and remained elevated, whereas that of adrenaline increased and then gradually reduced during the cold exposure (Papanek *et al.*, 1991).

In this study, severe hypertension developed in SHR groups exposed to both heat and cold environments. And the BPs of C-group and H-group in SHR were significantly high compared to that in N-group. In WKY, the exposure to cold environment induced the development of the hypertension, and that to hot reduced the BP. Therefore, the retardation of the development of genetic hypertension of SHR is expected after the exposure to hot environment. But, as shown in Fig. 5, the hypertension development was observed in the three groups of SHR. These results suggest that the development of hypertension in SHR is considerably tolerant to thermal environment influences and is somewhat different from WKY.

Susceptibility to the environmental stress in SHR

To investigate growth and the development of hypertension in SHR, Cierpial and McCarty (1987) studied maternal influences in SHR. The maternal environment before weaning affects growth and the development of hypertension in SHR. Cross fostering of SHR pups to WKY mothers resulted in reduction of BP and BW in adulthood compared to those in control SHR.

These facts suggest that the preweanling period is important for susceptibility of environmental influences.

In this study, before, the chronic exposure to various environmental temperatures at 1 month old, WKY and SHR rats used in this experiments were reared in the thermoneutral temperature. Though environmental stress were avoided in the preweanling period, clear different effects of environmental stress on the growth and the development of the hypertension were shown in this experiment. In next step, effects of environmental stress during the preweanling period should be studied.

CONCLUSION

In this study, chronic exposure to various environment temperatures began at 1 month old.

The results of this study suggest that although environmental temperature has similar affects on growth, an increase in body weight and tail in both SHR and WKY, it has different affects on the development of hypertension in these two strains. Furthermore, it scarcely affects the development of genetic hypertension in SHR. Hypertension developed in the three groups of SHR.

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