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Thermoregulatory Responses of Rabbits Impairing Pre-optic Hypothalamus by X-ray Irradiation

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Abstract: The time courses of the changes in peripheral vasodilation and in thermal panting induced by general heat exposure in unanesthetized PO/AH impaired rabbits closely resemble those observed in intact rabbits, although heat loss capability was slightly reduced. In the heat-acclimated PO/AH impaired rabbits, the level at which rectal temperature was regulated was higher than that in the cold-acclimated PO/AH impaired animals. The present findings that gains of heat dissipation to general heating increased in the heat-acclimated PO/AH impaired rabbits compared with these in the cold-acclimated PO/AH impaired rabbits were similar to those reported in thermally acclimated PO/AH intact rabbits. These results suggest that the thermal acclimation and temperature regulation system must be composed of hierarchically organized control loops located in thermosensitive tissues of central nervous axis.

Key words: Hypothalamus impaired rabbits, Thermoregulation, Thermal acclimation, Evaporative heat loss.

Results of previous experiment in sub-acute decerebrated rabbits indicated that those animals could respond to spinal thermal stimulation with adequate changes of activity of the autonomic thermoregulatory effectors (Kosaka *et al.*, 1975; Kosaka & Takaba, 1978). Among those thermally induced autonomic reactions of the unanesthetized decerebrated rabbits, changes in respiratory rate and peripheral vasomotor responses were most difficult to demonstrate presumably because it was more difficult, compared with intact rabbits, to maintain the decerebrated preparations in a reactive vasomotor state. In this experiment, therefore, the role of hypothalamic and extrahypothalamic deep body thermosensitivity in central mechanisms of temperature regulation (Simon, 1974) and thermal acclimation was precisely investigated in hypothalamus impaired rabbits by X-ray irradiation.

Experimental animals were six unanesthetized rabbits of which bilateral preoptic anterior hypothalamus (PO/AH) had been selectively impaired by *X*-ray irradiation of

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the three field technique (3000R: total). Between 30-60 days after X-ray irradiation, PO/AH impaired rabbits were exposed to general heat (Ta=40°C) and cold (Ta=15°C) environment. Temperatures of rectum (Tr), PO/AH (Th), reticular formation (Trf) and ear skin (Te) were continuously measured with thermocouples. Respiratory frequency (RR) was detected from the resistance changes of strain gauge. Local metabolism of PO/AH and reticular formation (RF) was measured by an electrical method with oxygen reducing electrodes, and was represented as the partial pressure of oxygen (Po_2) in the local cerebral tissues. Cerebral blood flow (C.B.F.) was calculated from the initial slope of the hydrogen clearance curves by using a basic computor (ATAC 450: Nihon Kohden Co.) (Kosaka & Ohwatari, 1982). The brain were embedded in paraffin and cut at about 10μ. The sections were stained with luxol fast blue and cresyl violet. In histological investigation, pycnosis and vascularization of the brain has occasionally been seen in irradiated animals. The experimental data were analyzed statistically by the student's t-test.

(I) Mean blood flow and local metabolism of intact PO/AH were 37-42ml/100g•min and 15-20mmHg (Po_2), respectively. Although these hypothalamic blood flows and

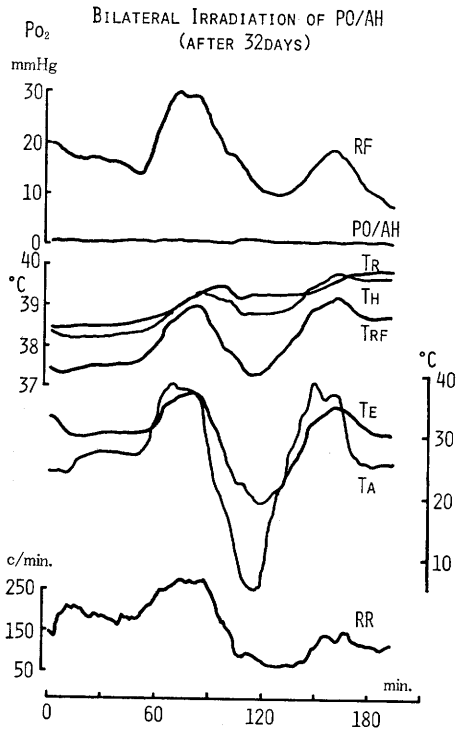

Fig. 1 (For details see text.)

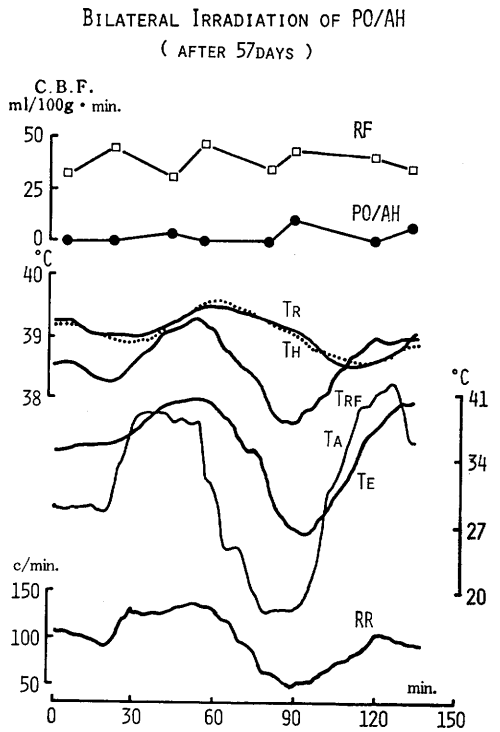

Fig. 2 (For details see text.)

metabolic activities observed in intact rabbits diminished or vanished in PO/AH impaired rabbits, the time courses of the changes in various autonomic thermoregulatory responses induced by general heating and cooling of the skin in these PO/AH impaired rabbits closely resembled those observed in PO/AH intact animals as demonstrated in Fig. 1 and Fig. 2. The experiments in these figures were performed in 32 days (Fig. 1) and 57 days (Fig. 2) after X-ray irradiation. Both rabbits could respond to external thermal stimuli with consistent changes of activity of thermoregulatory effectors, although the findings of Po_2 and cerebral blood flow (C.B.F.) in the PO/AH indicated that PO/AH activities distinctly vanished.

Table 1.

		Ta(°C) mean±SD	Tr(°C) mean±SD	Te(°C) mean±SD	RR(c/min) mean±SD
Intact rabbits (n=5)	Start of vasodilation	26.5±1.2	38.03±0.29	30.1±1.1	
	Maximum vasodilation	30.3±2.1	38.42±0.26	38.2±0.6	
	Start of increase of respiratory rate	32.8±1.9	38.31±0.36		130±27
	Maximum respiratory rate	36.6±1.3	39.12±0.31		420±41*
PO/AH-lesion rabbits (n=6)	Start of vasodilation	26.6±1.4	38.12±0.41	29.0±1.3	
	Maximum vasodilation	30.4±1.8	38.49±0.32	38.1±0.5	
	Start of increase of respiratory rate	31.8±2.0	38.38±0.29		120±45
	Maximum respiratory rate	35.8±1.5	38.85±0.69		340±52*

(For details see text.) *$p<0.05$ between 420 (c/min) and 340 (c/min)

(Ⅱ) Among various heat loss responses, capability of ear skin vasodilation and thermal panting were compared between intact and PO/AH impaired rabbits. Threshold temperatures of ambient air (Ta) and of rectum (Tr) for start and maximum of peripheral vasodilation and thermal polypnea of two groups of animals are summarized in Table 1. The difference of maximum respiratory rate between PO/AH intact rabbits (420 c/min) and PO/AH impaired rabbits (340 c/min) were statistically significant at the 5% ($p<0.05$) level, but significantly no difference was observed in peripheral vasodilation between two groups of rabbits. These results indicate that the lower brain stem is a site where thermal signals from the spinal cord can be transformed effectively into adequate drives controlling autonomic thermoregulatory effectors, especially the vasomotor tone of the cutaneous vessels and the ventilation of the upper respiratory tract connected with the preoptic anterior hypothalamus (Kosaka *et al.*, 1975; Kosaka & Takaba, 1978).

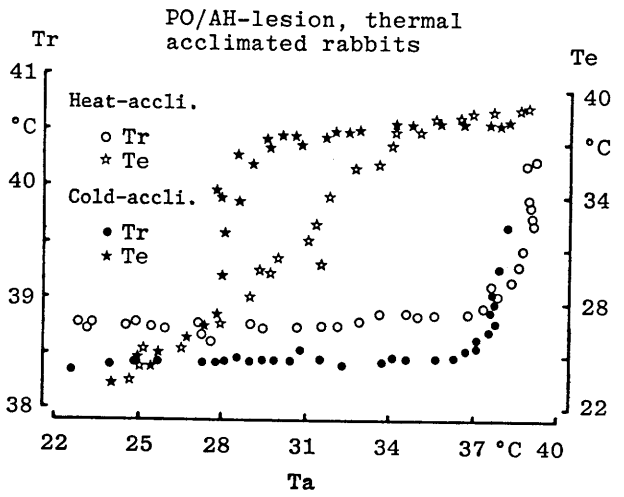

Fig. 3 (For details see text.)

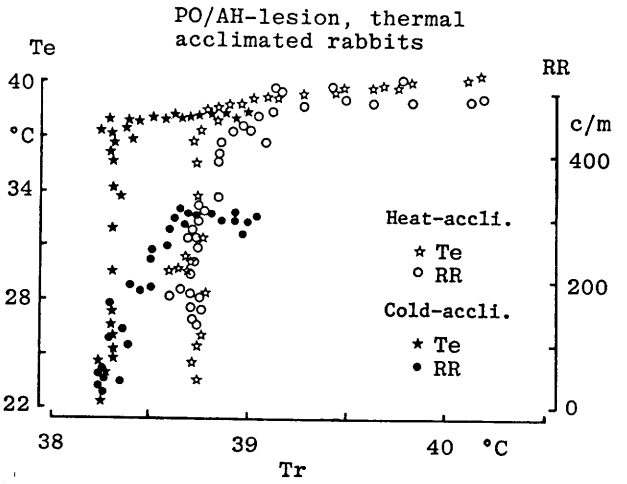

Fig. 4 (For details see text.)

(Ⅲ) Four animals out of another eight PO/AH impaired rabbits were thermally acclimated in heat environment (Ta=33°C) for 4 weeks and the rest 4 rabbits, in cold environment (Ta=10°C). As shown in Fig. 3 and Fig. 4, both PO/AH impaired heat-acclimated rabbits (the former) and PO/AH impaired cold-acclimated animals (the latter) were stepwise exposed to general heat environment (Ta=40°C). Changes in heat loss functions such as thermal panting (RR) and peripheral vasodilation (Te), and in rectal temperatures (Tr) induced by general heating were compared with both in the former and in the latter. In the former, rectal temperatures were always detected 0.3-0.4°C higher, and the threshold temperature for eliciting those heat loss responses also shifted

to higher level as compared with that in the latter. Gains of evaporative heat loss functions to general heating increased quantitatively in the former compared with those in the latter. The present findings agree with the experimental results in cold-acclimated guinea-pigs reported by Brück *et al.* (1970).

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X線照射による視床下部障害ウサギの体温調節反応

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X線多門照射による視床下部障害ウサギを用いて，暑熱刺激で誘発される末梢血管拡張や温熱性浅速呼吸（panting）などの熱放散反応について検索した。

視床下部障害ウサギの熱放散反応は，正常ウサギのそれと酷似であった。両群ウサギの末梢血管拡張には差を認めなかったが，panting による熱放散能は視床下部障害ウサギが正常ウサギより僅かに劣っていた。

視床下部障害ウサギを暑熱・寒冷に順化して上記の諸反応を比較したところ，(1)直腸温については寒冷順化ウサギより暑熱順化ウサギの方が高いレベルに調節されていた，(2)熱放散反応量に関しては暑熱順化ウサギは，寒冷順化ウサギより大きく，これは，暑熱・寒冷順化した視床下部無傷ウサギの結果と酷似であった。

これらの結果は，温度順化や体温調節反応系が，中枢神経幹内の温度感受性組織に局在する階層状調節機構によって形成される事を示唆している。

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