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Recovery of Thermoregulatory Function in Chronic Rabbit with Preoptic Area and Anterior Hypothalamic Lesions

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Abstract: The thermoregulatory responses to the continuous general thermal stimulation between 36℃ and 10℃ were observed in six rabbits with bilateral preptic area and anterior hypothalamus (PO/AH) lesions by electrolytic destruction. Series of experiments were performed on each rabbit, once before and five times after the operation of PO/AH lesions, and thermoregulatory ability in recovering process was investigated in rabbits with PO/AH lesions. (1) The body weights significantly decreased after PO/AH operation. But food intake (g/day) recovered to normal level at the 7th day after PO/AH operation and the body weights were over the preoperational level at the 18th day after PO/AH operation. (2) The PO/AH lesion caused marked impairment of abilities in heat loss responses such as vasodilation and thermal panting which lasted for 7 days after surgical operation. Therefore, general hyperthermia was successively induced, and rectal temperature (Tre) increased significantly in heat exposure. (3) Heat loss ability gradually recovered to the normal level by the 28th day after PO/AH operation, and Tre was controlled within normal range when the animal was exposed to heat exposure. (4) On the other hand, PO/AH lesion caused scarcely any disturbance of heat conservative function such as vasoconstriction. Therefore, no significant decrease in Tre was observed in PO/AH lesion rabbits, even in cold exposure.

These results suggest that extra PO/AH thermosensitive tissues in the posterior hypothalamus, midbrain reticular formation, medulla oblongata and spinal cord may join to play an important role of thermoregulation to general thermal stimulation within 28 days after bilateral PO/AH destruction in rabbits.

Key words: PO/AH lesion rabbit, Electrolytic destruction, Thermoregulation, Peripheral vasomotor response, Thermal panting

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Tre rapidly decreased due to effective heat loss in high Tea and RR during vasodilation and thermal panting. But decreasing Tre gradually leveled off by diminishing these heat loss responses and by successive appearance of vasoconstriction. And Tre was maintained at constant in the late of falling phase.

Thermoregulatory responses of a PO/AH lesion rabbit, the same animal in Fig. 3, were recorded at first day after operation (Fig. 4). In control phase, RR and Tea were similar to those before PO/AH lesion, though Tre was considerably higher. Increasing rate of Tea and increase of RR were slight, therefore Tre increased rapidly in rising and upper phase. The maximal RR was 186 min^{-1}. But heat conservative responses were induced as well as in case of before PO/AH lesion in falling and lower phase.

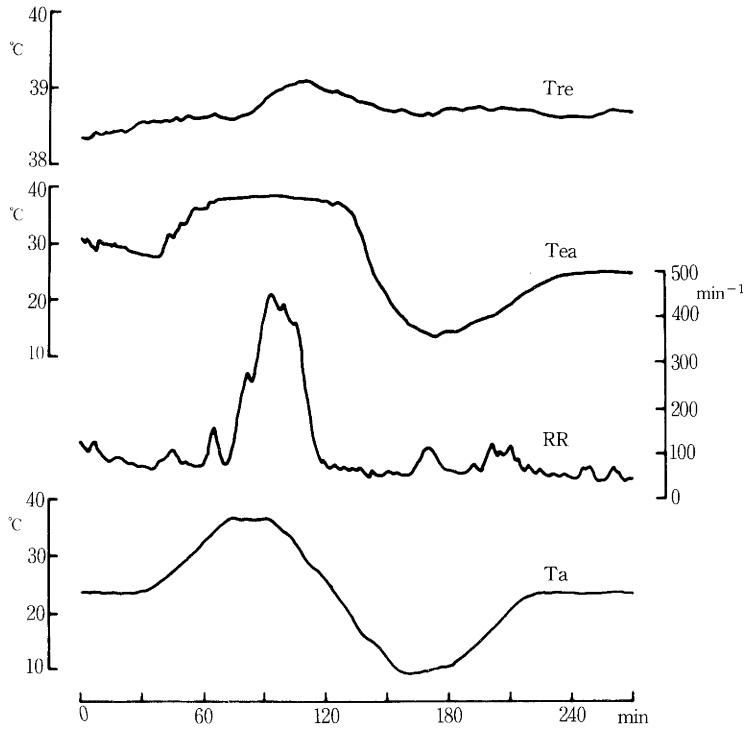

Fig. 3. The changes of rectal temperature (Tre), ear skin temperature (Tea) and respiratory rate (RR) by changing ambient air temperature (Ta) on a rabbit before PO/AH lesion.

Body temperature

Tre, Tea, Ta and RR of six rabbits in control phase are shown in Table 1. Tre at first day was significantly higher than Tre at before, and thereafter gradually decreased. There were no significant differences between stages in Tea and in RR.

Tre, Tea and Ta at maximal Tre of six rabbits during experiments at each stage are shown in Table 2. There was significant difference in Tre between before and first day after PO/AH operation. Also there was marked difference between first day and

seconds was applied to produce the electrolytic PO/AH lesion. The rabbits with the PO/AH lesions were reared under the same conditions as mentioned above.

Experimental procedure

An experiments for general thermal stimulation were carried out in an environmental chamber which can control according to preprogrammed temperature and humidity. The time course of changing ambient air temperature (Ta) was set on the program. Ta was controlled to 25℃ for 30 minutes (control phase), then increased to 36℃ for 30 minutes (rising phase). Ta at 36℃ was maintained for 30 minutes (upper phase), then decreased to 10℃ for 60 minutes (falling phase), and maintained at 10℃ for 30 minutes (lower phase). Again Ta was raised to 25℃ for 30 minutes (rising phase II), and maintained at 25℃ for 60 minutes (control phase II). The humidity was set at 60% during experiment.

The unanesthetized rabbit was put in the pillory not to press the neck and limbs were free. The experiment started when the rectal temperature (Tre), ear skin temperature (Tea) and respiratory rate (RR) of the rabbit were stable at 25℃ of Ta.

Each rabbit was submitted to a series of experiments: once before and five times after PO/AH operation (6 stages: 2 days before, first day, 3rd day, 7th day, 14th day and 28th day after).

Measurements

The body weights were measured at just before operation of the PO/AH lesion and experiments, and were compared with obtained body weights of six intact rabbits at the same period.

The thermistor probe for Tre was inserted into rectum to depth 12 cm, that for Tea was attached to the right ear and that for Ta was set aside 5 cm from the head. Tre, Tea and Ta were monitored every minute with a thermistor thermometer (K−270, Takara) and the data were automatically input to a computer (PC−8801, NEC) and were printed out. The curves of temperatures were displayed on the cathode ray tube visual display unit. RR was picked up from resistance changes of a strain−gauge input $ZnCl_2$ inside of silicone tube around the chest. RR were counted with another computer (ATAC−450, Nihon Koden Co.) and were printed out. The student t−test was used for the statistical estimation.

Histological Investigation

After experiments at 6 stages were completed in each rabbit, the animal was sacrificed with an overdose of sodium pentobarbital, and the brain was fixed with 10% formalin for one week. The sections, 6−9 μm thick, were cut from paraffin−embedded brain tissue and Hematoxylin Eosin stain was performed to determine the precise portion of the lesion.

RESULTS

The general thermal stimulation

The time courses of Ta and changing rate and time in each phase of actual measurements were: 24.78±0.35℃ (mean ± SD) for 30 minutes, +0.29℃/min for 38 minutes, 35.83±0.52℃ for 27 minutes, −0.43℃/min for 59 minutes, 10.24±0.62℃ for 28 minutes, +0.32℃/min for 43 minutes and 24.63±0.27℃ for 45 minutes, respectively. Thermoregulatory indicators and functional changes during programmed general thermal stimulation were actually analyzed by using the data of Ta mentioned above.

Histological findings

The histological investigations were performed in brains of all rabbits used for the present experiment. Fig. 1 shows the extent of the lesions produced in rabbits. In Fig. 1−A, a portion of bilateral PO/AH was completely omitted, and the marginal dark area indicated marked fibrotic degeneration with no blood supply which was further surrounded by degenerative tissues with moderate vascularization. Fig. 1−B shows degenerations of the extent of preoptic area to anterior hypothalamus above optic tract, which was the similar to that in area in Fig. 1−A.

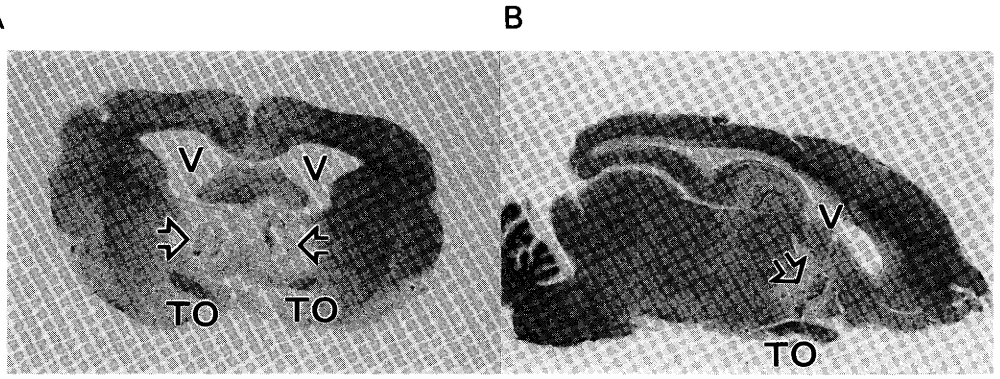

Fig. 1. Histological sections of 2 rabbit brains. Magnification: ×2.3; thickness: 7 μm; stain: hematoxylin eosin. A: frontal plane, 2.5 mm anterior to bregma. B: parasagittal plane, 1.6 mm lateral to midline. Illustrating typical lesions (arrow). V: lateral ventricle; TO: optic tract. (For details see text)

The changes of body weight

The rabbits drank only water at the first day after PO/AH operation. The amount of food and water consumed in a day began to increase slightly from 3rd day after PO/AH operation and reached to the preoperational level at 7th day after PO/AH operation.

The body weights of PO/AH lesion rabbits were compared with those of the intact six rabbit (Fig. 2). The mean body weight of six rabbits at just before the operations (W_0) was set at zero point. The differences of mean body weight at just before each

experiment from W_0 and the differences of mean body weights of six intact rabbits at the same period are shown. It is well known that the body weight of albino rabbit trends to increase up to about 3.5 kg. So the increase rate of body weight in the present intact rabbits was 0.02 kg/day. The W_0 of PO/AH lesion rabbits was 2.84±0.10 kg and that of intact rabbits was 2.73±0.08 kg. The difference of mean body weight of PO/AH lesion rabbits at first day from W_0 was −0.11±0.04 kg. Decreasing body weight was observed within 7 days after surgical operation, then body weight increased. And there were not significant diffrences between increase rates (kg/day) in PO/AH lesion rabbits after 7 days and those of intact rabbits. Nevertheless, body weights of the former did not reach to those of the latter.

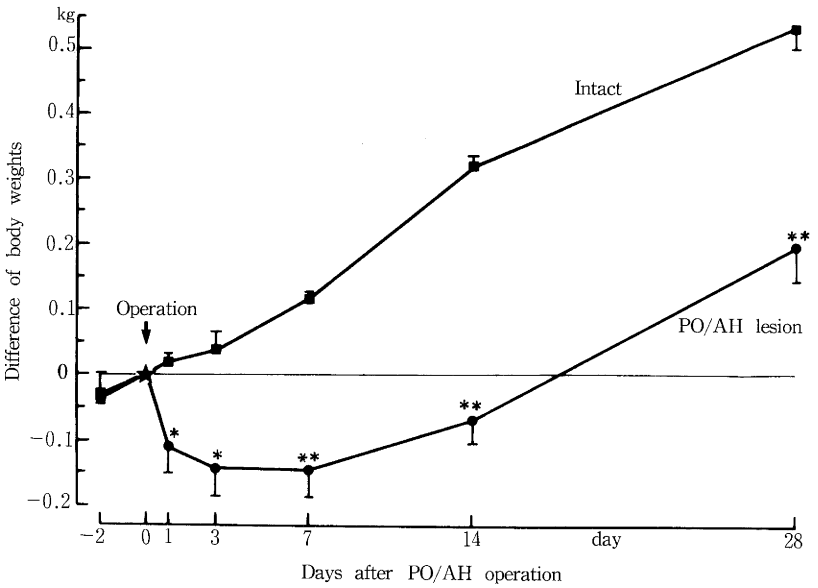

Fig. 2. Comparison of body weight changes at each stage between intact rabbits (N=6; square) and PO/AH lesion rabbits (N=6; circle). Mean ± SE and * $p<0.05$, ** $p<0.01$ compared with value of intact rabbits at same stage. (For details see taxt)

Examples of experiments

Thermoregulatory responses of a single rabbit before PO/AH lesion in this experiment are shown in Fig. 3. Tre, Tea and RR were stable in control phase. The first, increase of Tea due to vasodilation was induced in the rising phase. The next, evaporative heat loss by rapid shallow respiration (thermal panting) was observed at initial in the upper phase and maximal RR was 433 min^{-1}. After these heat loss abilities were beyond maximal efficiency, Tre increased rapidly. Increase in Tre continued for some minutes in spite of in falling phase. In this falling phase, Ta decreased still more,

INTRODUCTION

Bazett and Penfield (1922) reported that hypothalamus has an important role in thermoregulation from the experiment with decerebrated cats. Ranson and Magoun (1939) studied the functions of hypothalamus with electric stimulations and localized lesions in cats, dogs and monkeys, and showed that PO/AH lesions caused impairment of thermoregulation against both heat and cold. In recent reports, it is recognized that lesions in PO/AH cause impairment of thermoregulation against heat and lesions in posterior hypothalamus cause impairment of thermoregulation against cold. However, there were also reports that lesions in PO/AH caused disturbances in thermoregulation against both heat and cold (Satinoff and Shan, 1971; Lipton *et al.*, 1974). The different responses were induced by the slight difference of position of lesions in hypothalamus (Blatteis and Banet, 1986). Most of these experiments were performed on cats and rats, but studies on rabbits are very scarce cases.

Nakayama *et al.* (1963) recorded the activity of thermosensitive neuron in PO/AH of anesthetized cat and denoted that impulse rate increases at increasing local temperature. Thereafter, it was considered that thermoceptive and controlling functions were residing in hypothalamic structures (Hammel *et al.*, 1960; Cooper, 1966). However, medulla oblongata and spinal cord also have the same function was evidenced (Cabanac, 1975; Kosaka *et al.*, 1967; Thauer, 1970). Later on, it was considered that the thermoregulation is due to the hierarchical control (Simon, 1974).

The purpose of this study is to test whether bilateral PO/AH lesions in rabbits cause disturbance of thermoregulation against heat and/or cold, and to elucidate whether it is a permanent or transient disturbances.

MATERIALS AND METHODS

Animals

Twenty−two male albino rabbits were used in this study. Six rabbits with complete lesions in PO/AH of them weighed 2.77±0.31 kg (Mean ± SD) at start of series of experiments. The rabbits were reared in an environmental controlled room at temperature of 25± 2 ℃, at humidity of 60± 5 % and 12:12 light and dark photoperiod. The food and water were controlled with 150 g and 500 ml per day, respectively.

Electrolytic lesion

A steel electrode was used to produce electrolytic lesions at bilateral PO/AH in rabbits. The electrode was 1 mm in diameter and 1.5 mm uninsulated tip. All the operations were performed aseptically. The rabbit was anesthetized with sodium pentobarbital (10 mg/kg) injected intravenously to the ear. The head of rabbit was fixed into the stereotaxic instrument. Bilateral PO/AH lesions were made at 2.5 mm anterior to the bregma, either 1.5 mm lateral to the midline and 14 mm under the skull surface level (Fifková and Maršala, 1967). The indifferent electrode of an Ag plate of 15 mm in diameter was placed on the muscle in the neck. The direct current of 5 mA for 20

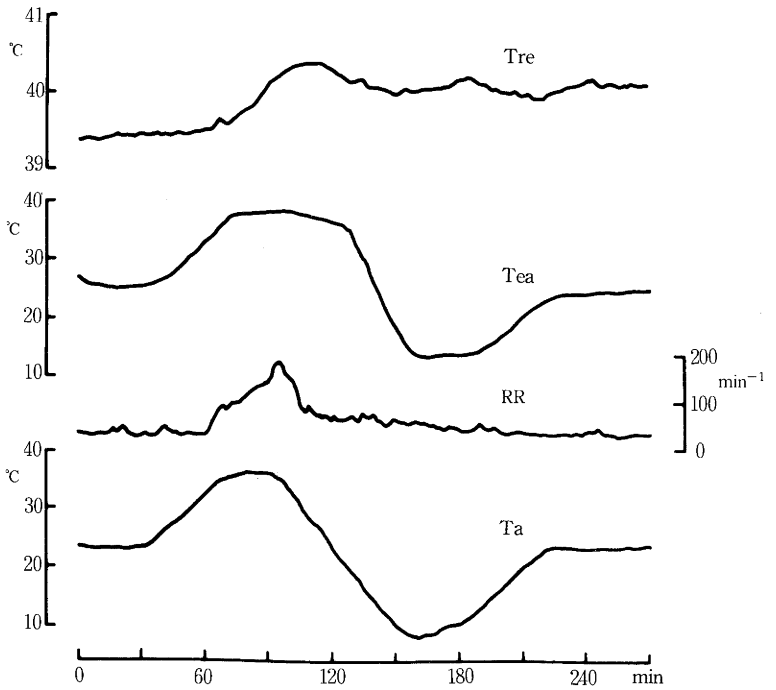

Fig. 4. The changes of rectal temperature (Tre), ear skin temperature (Tea) and respiratory rate (RR) induced by changing ambient air temperature (Ta) on the rabbit at the first day after PO/AH operation.

Table 1. Comparison of Tre, Tea RR and Ta in contol phase at each satge of PO/AH lesion in six rabbits

Stage	Tre (°C)	Tea (°C)	RR (min^{-1})	Ta (°C)
Before	38.34 ± 0.13	28.77 ± 0.93	89 ± 19	24.42 ± 0.20
First day	39.23 ± 0.33*	29.29 ± 1.47	80 ± 35	24.53 ± 0.28
3rd day	38.50 ± 0.15	29.97 ± 1.63	95 ± 36	24.71 ± 0.40
7th day	38.47 ± 0.05	30.54 ± 1.56	84 ± 38	24.43 ± 0.30
14th day	38.39 ± 0.12	27.68 ± 0.86	65 ± 9	24.32 ± 0.27
28th day	38.38 ± 0.18	26.34 ± 0.41	77 ± 18	24.48 ± 0.24

Mean±SE, * $p<0.05$ compared with value before

Table 2. Cpmparison of Tre, Tea and Ta at maximal rectal temperature at each stage of PO/AH lesion in six rabbits

Stage	Tre (°C)	Tea (°C)	Ta (°C)
Before	38.83 ± 0.08	37.55 ± 0.31	31.07 ± 1.45
First day	40.06 ± 0.34**	37.96 ± 0.56	31.84 ± 0.61
3rd day	39.15 ± 0.15	38.12 ± 0.14	31.93 ± 0.53
7th day	39.18 ± 0.17	37.86 ± 0.21	30.18 ± 0.57
14th day	39.00 ± 0.13*	36.88 ± 0.53	30.92 ± 0.99
28th day	38.84 ± 0.17*	37.47 ± 0.26	30.45 ± 0.86

Mean ± SE, ** $p<0.01$ compared with value before
* $p<0.05$ compared with value at first day

14th day as well as 28th day. Though Ta started to decrease in falling phase, Tea was still high due to high Tre at each stage.

The mean and SE of minimal Tre in each stage was 38.23±0.12℃ at before, 39.00±0.82℃ at first day, 38.26±0.10℃ at 3rd day, 38.19±0.12℃ at 7th day 38.20±0.12℃ at 14th day and 38.16±0.18℃ at 28th day, respectively. Differences in Tre among these values were not significant. The minimal Tre in each rabbit was observed not only in falling phase but in lower phase, rising phase II, control phase II and initial in rising phase.

Table 3. Comparison of Tre, Tea and Ta at leveling off the decrease of rectal temperature due to vasoconstriction at each stage of PO/AH lesion in six rabbits

Stage	Tre (°C)	Tea (°C)	Ta (°C)
Before	38.43 ± 0.15	17.76 ± 2.03	11.47 ± 1.55
First day	39.23 ± 0.38	18.13 ± 1.07	15.20 ± 2.25
3rd day	38.58 ± 0.11	18.32 ± 1.34	11.41 ± 0.65
7th day	38.20 ± 0.20	17.82 ± 1.25	11.86 ± 0.72
14th day	38.36 ± 0.18	15.88 ± 1.22	10.04 ± 0.45
28th day	38.30 ± 0.17	19.59 ± 2.54	12.22 ± 1.02

Mean ± SE

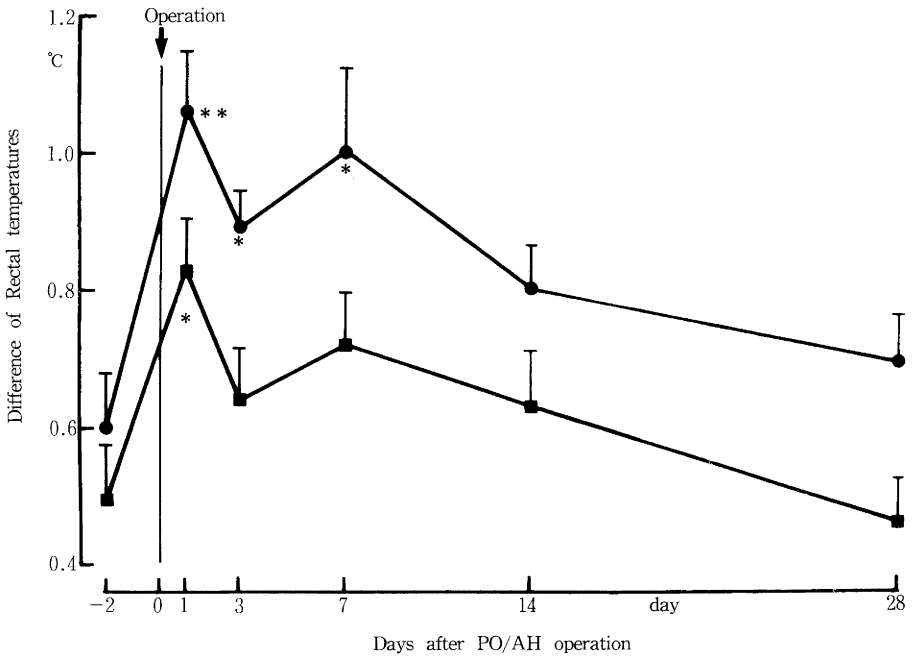

Fig. 5. The difference of maximal and minimal rectal temperatures (circle) during thermal stimulation and the difference of maximal rectal temperature and the mean rectal temperature in control phase (square) in experiment in six rabbits after PO/AH operation. Mean ± SE and * $p<0.05$, ** $p<0.01$ compared with each values on 2 days before PO/AH lesion. (For details see text)

Tre, Tea and Ta are shown in the Table 3 when decrease of Tre ceased at late in falling phase or initial in lower phase due to heat conservative responses. There were not significant differences among these values.

Rectal temperature differences (ΔTre) between in control phase and maximum, and ΔTre between maximum and minimum are shown in Fig. 5. Concerning ΔTre between maximum and minimum: ΔTre at first day, 3rd day and 7th day were significantly larger than ΔTre of before PO/AH lesion. Regarding ΔTre between in control phase and maximum: ΔTre of before and at fist day was significantly different. The changes of these two lines show the same pattern.

The vasodilation and vasoconstriction in the ear skin.

The vasodilation in ear skin of all rabbits were induced in rising phase at all stages. Tre, Tea and Ta at the onset of vasodilation at each stage are shown in Table 4. Tre at first day was significantly high but later on gradually decreased to Tre before PO/AH lesion.

The vasoconstriction in ear skin of all rabbits were also induced in falling phase at all stages. Tre, Tea and Ta at the onset of vasoconstriction at each stage are shown in Table 5. Tre at first day was significantly high compared with Tre before operation.

Table 4. Comparison of Tre, Tea and Ta at onset of vasodilation in the ear at each stage of PO/AH lesion in six rabbits

Stage	Tre (°C)	Tea (°C)	Ta (°C)
Before	38.27 ± 0.09	30.90 ± 0.46	29.10 ± 0.80
First dyay	39.30 ± 0.36*	31.38 ± 0.41	30.00 ± 0.57
3rd day	38.55 ± 0.13	31.93 ± 0.84	30.02 ± 0.85
7th day	38.44 ± 0.06	32.38 ± 0.47	30.50 ± 0.95
14th day	38.42 ± 0.24	31.45 ± 0.44	30.81 ± 1.02
28th day	38.29 ± 0.11	30.96 ± 0.40	31.04 ± 0.52

Mean ± SE, * $p>0.05$ compared with value before

Table 5. Comparison of Tre, Tea and Ta at onset of vasoconstridtion in the ear at each stage of PO/AH lesion in six rabbits

Stage	Tre (°C)	Tea (°C)	Ta (°C)
Before	38.55 ± 0.08	35.08 ± 0.20	20.44 ± 0.64
First day	39.75 ± 0.34*	34.62 ± 0.23	20.02 ± 1.19
3rd day	38.82 ± 0.10	34.55 ± 0.65	20.67 ± 1.28
7th day	38.86 ± 0.12	34.44 ± 0.46	17.91 ± 1.48
14th day	38.71 ± 0.08	34.58 ± 0.29	21.78 ± 1.39
28th day	38.61 ± 0.12	33.87 ± 0.38	20.13 ± 1.00

Mean ± SE, * $p<0.05$ compared with value before

Regression coefficients of Tea on Ta (RC) in rising phase and falling phase at each stage are shown in Fig. 6. The increasing rate of Ta in rising phase was 0.29 ℃/min and the decreasing rate of Ta in falling phase was 0.43℃/min. For the calculation of RC in vasodilation, the data obtained from the most rapid increase of Tea were used. In falling phase, while vasodilation was continuously, Tea slightly decreased as a result of decreasing Ta without vasoconstriction. After that, rapid decrease of Tea was induced by vasoconstriction, the data in this term were analyzed as the RC in vasoconstriction. The RC in vasodilation at first day, 3rd day, 7th day and 14th day were significantly lower than RC before PO/AH operation. The rapid increase of Tea by vasodilation was not observed up to the 14th day after PO/AH operation. Concerning RC in vasoconstriction, RC at all stages after PO/AH operation were lower than RC before PO/AH lesion, but there were not significant differences among these values.

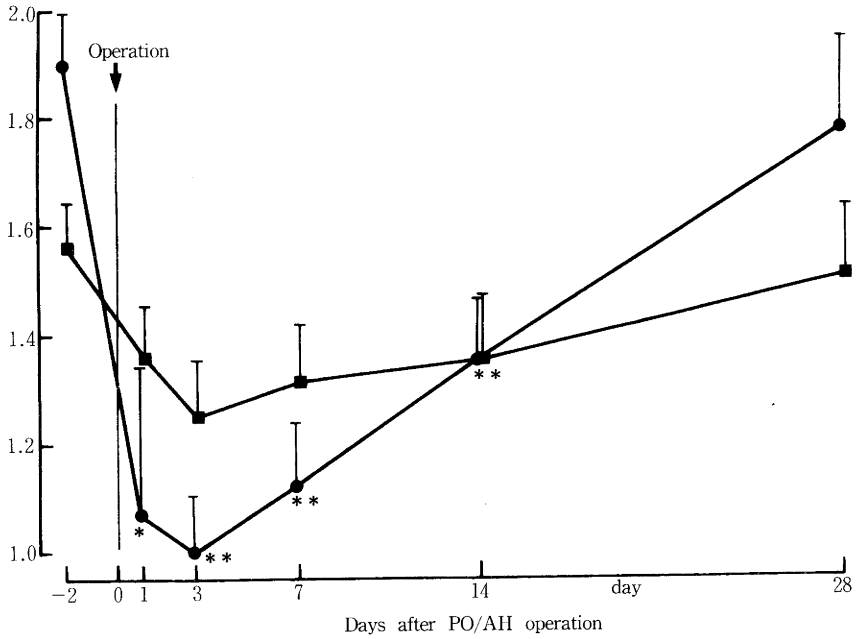

Fig. 6. The regression coefficients of ear skin temperature on ambient air temperature for increasing ear skin temperature by vasodilation (circle) and decreasing ear skin temperature by vasoconstriction (sequare) after PO/AH operation in six rabbits. Mean ± SE and * $p<0.05$, ** $p<0.01$ compared with value on 2 days before PO/AH lesion. (For details see text)

The evaporative heat loss by respiration

RR, Tre, Tea, and Ta at maximal RR during experiment in six rabbits at each stage are shown in Table 6. The maximal RR at first day, 3rd day, 7th day and 14th day were significantly low compared with value before PO/AH lesion. Tre at first day was significantly higher than Tre at the other stages.

The maximal RR, mean RR in control phase and minimal RR during experiment are shown in Fig. 7. There were no significant differences between stages in minimal RR and mean RR in control phase.

Table 6. Comparison of RR, Tre, Tea and Ta at maximal respiratory rate the at each stage of PO/AH lesion in six rabbits

Stage	R.R. (min^{-1})	Tre (°C)	Tea (°C)	Ta (°C)
Before	433 ± 18	38.70 ± 0.09	37.94 ± 0.11	35.35 ± 0.35
First day	173 ± 18**	39.96 ± 0.34*	38.26 ± 0.51	32.66 ± 1.07
3rd day	231 ± 52**	38.91 ± 0.15	38.01 ± 0.44	35.30 ± 0.69
7th day	270 ± 46*	39.00 ± 0.13	38.13 ± 0.19	34.12 ± 0.56
14th day	290 ± 42*	38.83 ± 0.13	37.86 ± 0.16	34.54 ± 0.64
28th day	350 ± 34	38.69 ± 0.17	37.65 ± 0.25	35.74 ± 0.55

Mean ± SE, * $p<0.05$ and ** $p<0.01$ compared with value before

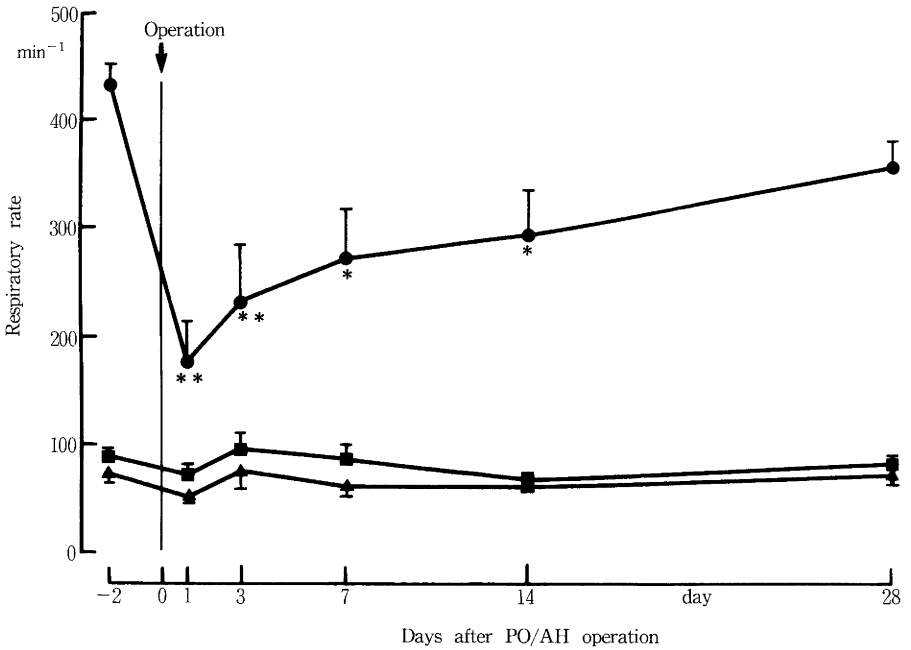

Fig. 7. The maximal (circle) and minimal (triangle) respiratory rates during thermal stimulation, and the mean respiratory rate (square) in control phase before and after PO/AH operation in six rabbits. Mean ± SE and * $p<0.05$, ** $p<0.01$ compared with each value on 2 days before PO/AH lesion. (For details see text)

DISCUSSION

The body weight decreased until 7 days after PO/AH operation, which was mainly caused by a little amount of food intake. Further, the influence of high body temperature may be considered. The body weight recovered to preoperational level at 18 th day after PO/AH operation. These present phenomena support the result in rats reported by Satinoff and Shan (1971).

At first day in neutral Ta, Tea and RR were not so high values in spite of significant high level in Tre compared with before PO/AH lesion. This suggests that lesion in the PO/AH caused impairment of heat loss mechanism. According to Lipton *et al.* (1974), Tre in rats with PO/AH lesions at 23℃ of Ta was higher than that before PO/AH lesion. Ranson and Magoum (1939) already reported similar result in cats. But the rats with PO/AH lesions had a higher resting Tre and lower tail skin temperature than the rats with control PO/AH operation, but difference was not significant in the report of Thompson and Stevanson (1965). So it is presumed that elevated Tre at first day might be caused not only the the PO/AH lesion but the operational precedure itself.

ΔTre between maximum and minimum were significantly large at first day, 3rd day and 7th day after PO/AH operation. In Fig. 5, the upper line was changes in ΔTre between maximum and minimum due to heat and cold exposures and lower line was changes in ΔTre between control value and maximum due to heat exposure. Therefore difference of these two lines at the same stage was decrease in Tre by cold exposure, and there were not significant differences among these values at each stage. This suggests that large ΔTre during thermal stimulation in the rabbit with PO/AH lesion was due to increase of Tre in heat exposure.

In the cause of impairment of heat loss mechanism, Tre after PO/AH destruction increased markedly in heat exposure. Tre at the onset of vasodilation was significantly high at first day after PO/AH operation compared with that before PO/AH lesion but decreased day by day (see Table 4). On the other hand, the regression coefficients of Tea on Ta during vasodilation were low about one, which indicated that increasing Tea considerably depended on change of Ta, so the most extent of heat loss ability was deprived by PO/AH lesion. However, at 28th day after PO/AH operation, this ability already recovered to the preoperational level (see Fig. 6).

Hales and Findely (1968) reported that the thermal panting caused almost a 4−fold increase in respiratory minute volume, but there was no appreciable change in oxygen consumption. It is well known that thermal panting is important for heat loss in the rabbit. However, the evaporative heat loss with respiration was not so effective until 14th day after PO/AH operation in the present experiment, because rapid shallow respiration was not observed (see Table 6 and Fig. 7).

During cold exposure in falling and lower phases, decrease in Tre ceased and Tre was controlled at certain level in spite of after PO/AH operation, because the heat conservation was induced as well as before PO/AH lesion. The level of controlled Tre at each stage was almost the same as that before PO/AH lesion (Table 3). Tre at onset of

vasoconstriction in the ear was significantly high at first day after PO/AH operation (Table 5). However, in the present experiment, since Tre at onset of vasoconstriction was detected in falling phase after heat load at 36℃ of Ta in upper phase, temperature difference of Tre at onset of vasoconstriton from maximal Tre was not statistically significant in each stage. And there were not significant differences among RC during vasoconstriction in each stage (Fig. 6). Therefore the ability of heat conservation due to the vasoconstriction was not reduced by PO/AH lesion.

In this study, the bilateral PO/AH lesions in the rabbit caused disturbance of the body temperature regulation against heat but almost no impairment of that against cold in the continuous general thermal stimulation between 36℃ and 10℃. In rabbits with bilateral PO/AH lesions by X−ray irradiation, Ohwatari *et al.* (1983) obtained the similar result, and the temperature in impaired PO/AH changed slowly compared with the temperature of midbrain with the central thermal sensitive tissue due to lack of blood supply. Han and Brobeck (1961) reported that lesions in PO/AH caused impairment of heat loss mechanisms but no disturbance of regulation against cold from the result of exposed 12 rats with bilateral PO/AH lesion at 34℃ for 45 minutes and at 5.5℃ for 2 hours. In goats with bilateral PO/AH lesion by proton irradiation, the heat−dissipation threshold raised and the threshold of shivering in Ta falled (Andersson *et al.*, 1965). On the other hand, there are also reports that the bilateral PO/AH lesion in rats caused disturbances in regulation against both heat and cold (Satinoff and Shan, 1971; Lipton *et al.*, 1974). The differences of these results might be influenced by the area and grade of brain lesion, method of stimulation and animal species.

Today, it is reported that the thermoreceptors exist in many regions: in the skin (Hensel, 1973), in abdomen (Rawson and Quick, 1970), in spinal cord (Simon *et al.*, 1964; Meurer *et al.*, 1967; Simon and Iriki, 1971; Jessen and Simon−Oppermann, 1976), in medulla oblongata (Cabanac, 1975; Murakami and Sakata, 1978), in midbrain (Nakayama and Hardy, 1969) and in PO/AH (Nakayama *et al.*, 1963). And the thermoregulation was controlled by the multiplicative integration of thermal inputs from hypothalamus and extra hypothalamus (Hori, 1979). The contributions of thermal input from each region in the body are difference for thermoregulatory responses, and the contribution of each region differs in species. The contribution of PO/AH to the heat loss responses generally dominates in mammals. The hypothalamus has important role for thermoregulation in mammals, however the roles of midbrain (Hori and Harada, 1976), medulla oblongata (Lipton, 1973; Chai and Lin, 1973) and spinal cord (Kosaka *et al.*, 1967; Kosaka *et al.*, 1969; Thauer, 1970; Simon, 1974) for thermoregulation were reported. The oxygen consumption increased by cold stimulation of spinal cord in decerebrated rabbits (Kosaka *et al.*, 1984). It is generally considered that the ability of thermoregulation is not only in the hypothalamus but also in those regions and the thermoregulation is due to the hierarchical control.

In the present study, the ability of heat loss reduced until 14th day after PO/AH lesion, thereafter recovered day by day, and reached to the preoperational level at 28th

day after PO/AH destruction. From the present results, it is concluded that thermoregulatory function against heat load is reduced by PO/AH lesion in the rabbit, but dormant or weak contribution of warm signal input from extra PO/AH in central nervous and deep body thermosensitive tissues gradually rise and grow up until one month after PO/AH surgical operation.

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慢性視床下部障害ウサギの体温調節能の回復過程に関する研究

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22羽のウサギの視束前野・前視床下部（PO/AH）を電気破壊して，破壊後1日目・3日目・7日目・14日目・28日目に，36℃から10℃の連続した全身皮膚温度刺激を加え，体温調節能を検索し，破壊前値と比較検討した．典型的なPO/AH破壊が認められた6羽について，体温調節能の回復過程を解析し，下記の結果を得た．

(1) PO/AH破壊により，食物摂取量は減少し，体重は7日目まで有意に減少した．以後，食物摂取量の増加に伴い，体重は徐々に増加した．

(2) PO/AH破壊後1日目の25℃における安静時の直腸温は，破壊前の値に比し有意に高かった．

(3) PO/AH破壊により，耳介の皮膚血管拡張や浅速呼吸による熱放散能力が障害を受け，暑熱暴露に対し直腸温は有意に上昇した．しかし，熱放散能力は徐々に回復し，破壊後28日目には，直腸温の上昇は破壊前値に比し有意の差は認められなかった．

(4) PO/AH破壊により，耳介の皮膚血管収縮による熱放散抑制能力は障害を受けず，寒冷暴露に対し直腸温は僅かに下降した．

PO/AH破壊により，暑熱に対する体温調節能は一過性の障害がみられたが，この機能障害は1ケ月後回復した．その回復は，後視床下部・中脳・延髄・脊髄など PO/AH 以外の温度感受性組織と，これ等組織の統合機能の関与が，増大してきた結果と考えられる．

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