LOWERING OF THE BODY TEMPERATURE INDUCED BY VASOPRESSIN

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In our previous studies1-3) it was shown that the secretion of antidiuretic hormone (ADH) from the posterior pituitary lobe is also induced by heat exposure. Ueno4) who investigated histological changes in the neurohypophysis of rats exposed to heat and cold, noted that heat exposure caused severe changes in the pituicytes and interstitial structures of the posterior lobe, and that the changes were more marked in rats in which no particularly high body temperature developed during heat exposure than those with considerably elevated body temperature. The finding may suggest that the ADH plays a role in the regulation of the body temperature in animals exposed to heat, but little is yet known as to the effect of posterior pituitary hormone on the body temperature. The present experiments demonstrated that vasopressin, either exogenous or endogenous, caused a prompt fall in the body temperature, acting possibly peripherally. However, vasopressin was ineffective in inhibiting the rise of body temperature provoked by heat exposure.

METHODS

Animals used in the experiments were male Wister rats, weighing 150 to 200 g. They were kept at a constant temperature of 20°C and fed on rat biscuits and water ad lib. Using an electrothermometer the rectal temperature was measured at 10-minute intervals at a depth of 5 cm from the external anal orifice.

Posterior pituitary hormones employed were Pitressin (Parke, Davis & Co.), Pitocin (Parke, Davis & Co.), synthetic lysine vasopressin (Sandoz) and Syntocinon (Sandoz) which were diluted with the physiological saline and injected intraperitoneally or intravenously into the tail vein. Hypertonic solutions of 8.5 per cent sodium chloride and 2M sucrose warmed at 38°C were infused at a rate of 0.1 ml per minute into the left common carotid artery through a polyethylene cannule inserted.

Electrolesions were made in the anterior hypothalamic area bilaterally by means of electrolysis with a direct current of 2 mA for 15 seconds and the animals were used 24 to 48 hours after the operation. Hypophysectomy and neurohypophysectomy were...
performed by approaching the pituitary parapharyngeally under hexobarbital anesthesia. The rats were treated with Aureomycin (Lederle) to prevent postoperative infection and used 7 to 10 days after the surgery. After the experiment completeness of the surgery was examined by inspection.

Phenoxybenzamine hydrochloride (Dibenzylin; Smith, Kline & French Labs.) was injected intravenously in a dose of 2 mg per 100 g body weight 18 hours prior to the experiment, and atropine sulfate in a dose of 0.1 mg per 100 g injected subcutaneously 1 hour before the experiment.

In the experiment of heat exposure rats were subjected to a high ambient temperature of 40°C for 40 minutes.

RESULTS

1. Effect of the injection of posterior pituitary hormone. When Pitressin was injected intraperitoneally in doses ranging from 20 to 400 mU per 100 g body weight into normal rats, the rectal temperature immediately began to fall and reached the lowest level about 30 minutes after the injection; then it tended to rise toward the pre-injection level. The larger the dose of Pitressin was given, the larger the fall in the body temperature was resulted. Pitressin in a dose of 10 mU was ineffective in causing the change (Fig. 1). Synthetic lysine vasopressin caused a similar lowering of the rectal temperature, indicating that the change is not due to contaminants in the posterior pituitary extract (Fig. 2). Pitocin and Syntocinon, even in a dose of 400 mU per 100 g, did not affect the body temperature (Fig. 1 and 2).

If Pitressin was injected intravenously, the rectal temperature was lowered

![Graph](image-url)

**Fig. 1.** Effect of intraperitoneal injection of Pitressin and Pitocin on the rectal temperature in normal rats. Numbers in parentheses indicate number of rats in each experiment.
and reached the lowest level about 20 minutes after the injection. In this case the minimum effective dose was 10 mU (Fig. 3).

2. Effect of intracarotid infusion of hypertonic solutions. To examine whether endogenous vasopressin released from the posterior lobe exhibits the same effect in causing the fall in the body temperature as observed after exogenous vasopressin, hypertonic solutions were infused at a rate of 0.1 ml per minute into the common carotid artery. The infusion of 0.5 ml of 8.5 per cent sodium

![Graph](image-url)  
**FIG. 2.** Effect of intraperitoneal injection of synthetic lysine vasopressin and Syntocinon on the rectal temperature in normal rats.

![Graph](image-url)  
**FIG. 3.** Effect of intravenous injection of Pitressin on the rectal temperature in normal rats.
chloride or 2 M sucrose solution resulted in a distinct fall in the rectal temperature, while that of isotonic solutions had no effect on it. It was also shown that the intravenous infusion into the tail vein did not cause any change in the body temperature (Fig. 4).

In hydrated rats the intracarotid infusion of 8.5 per cent sodium chloride caused a significant decrease in the urine output to 69 per cent of the control

Fig. 4. Effect of intracarotid (upper) and intravenous (lower) infusions of hypertonic solutions on the rectal temperature in normal rats.

Fig. 5. Effect of intracarotid infusion of hypertonic saline on the rectal temperature in neurohypophyssectomized rats.
value. Neither intracarotid infusion of 0.85 per cent sodium chloride nor intravenous infusion of 8.5 per cent solution caused any significant alteration in the urine excretion rate.

The results indicate that the endogenous vasopressin released in response to hypertonicity of the circulating body fluid is capable of lowering the body temperature. This inference was supported by an observation in neurohypophysectomized rats which did not store the ADH. As shown in Fig. 5, in these diabetes insipidus rats the rectal temperature did not change at all following intracarotid infusion of 8.5 per cent sodium chloride solution.

3. Effect of vasopressin on the elevation of body temperature provoked by heat exposure. It was shown that the release of ADH was stimulated on exposure of animals to heat1-9. Since vasopressin was capable of lowering the body temperature as demonstrated above, ADH released by heat exposure may play a regulatory role in the body temperature in animals under a hot environment, which usually caused its elevation.

Rats with lesions in the anterior hypothalamic area and neuro- and totally hypophysectomized rats were exposed to a high ambient temperature of 40°C for 40 minutes. As shown in Fig. 6, the body temperature of neurohypophysectomized rats as well as that of totally hypophysectomized ones elevated to the same level at the same rate as observed in the control rats, making the possibility less probable that the release of stored vasopressin may suppress

![Fig. 6. Effect of heat exposure on the rectal temperature in rats with anterior hypothalamic lesions, neurohypophysectomized (NHX) and totally hypophysectomized (THX) rats.](image-url)
the rise of body temperature. On the other hand, in rats with anterior hypothalamic lesions the rectal temperature rose to a high level over 40°C on exposure to the same heat conditions.

Subcutaneous injection of Pitressin tannate in oil in a dose of 500 mU per 100 g body weight caused a prolonged fall in the body temperature. The injection of this preparation may be expected to influence the body temperature elevation due to heat exposure. However, it did not exhibit any suppressing effect on it both in normal and neurohypophysectomized rats subjected to heat exposure (Fig. 7). From the results it is inferred that vasopressin does not participate in the regulation of body temperature in animals exposed to heat.

4. Action site of vasopressin. Vasopressin may affect the heat center in the anterior hypothalamus, either increasing heat loss or reducing heat production. To know the central action of the hormone, Pitressin was infused in doses of 2 and 10 mU into the carotid artery through a polyethylen tube. The effects were compared with those of the infusion into the jugular vein at the same rate in the same doses. As shown in Fig. 8, the fall in the rectal temperature following intracarotid infusion was the same in both the time course and the extent as that following intravenous infusion.

In the next series of experiments 10 mU of Pitressin per 100 g body weight was injected intravenously into rats with anterior hypothalamic lesions and into neuro- and totally hypophysectomized rats. In the lesioned rats in which the heat center had been probably damaged the injection of Pitressin resulted in a fall in the body temperature to the same extent as in the controls (Fig. 9).

![Fig. 7. Effect of Pitressin tannate on the body temperature rise due to heat exposure in normal and neurohypophysectomized (NHX) rats.](image-url)
Neurohypophysectomized rats and totally hypophysectomized ones also showed a similar response to exogenous Pitressin to that seen in the controls.

To examine whether the autonomic nervous function is involved in the manifestation of the effect of vasopressin, sympathetic or parasympathetic nervous activity was blocked by Dibenzylin or atropine respectively. However,

**Fig. 8.** Effect of intravenous (upper) and intracarotid (lower) infusions of Pitressin on the rectal temperature in normal rats.

**Fig. 9.** Effect of intravenous injection of Pitressin on the temperature in rats with anterior hypothalamic lesions, neurohypophysectomized (NHX) and totally hypophysectomized (THX) rats.
FIG. 10. Effect of phenoxybenzamine and atropine on the fall of the rectal temperature following Pitressin.

The present experiments demonstrated that the administration of vasopressin even in relatively small doses caused a prompt fall in the body temperature. According to Verney\(^5\), intracarotid infusion of hypertonic solution stimulates the release of vasopressin from the posterior pituitary lobe. In the present experiment the infusion of hypertonic saline and sucrose solutions into the common carotid artery caused a significant lowering in the rectal temperature in normal rats, but not in neurohypophysectomized ones. A similar infusion into the tail vein had no effect. These facts indicate that the endogenous vasopressin is also capable of lowering the body temperature.

The effect of intracarotid infusion of vasopressin on the body temperature was the same in both the time course and the extent of the fall as that of intravenous infusion. The body temperature lowering effect of the hormone was also observed in rats with anterior hypothalamic lesions in which the heat center had been damaged. These results suggest that vasopressin does not act on the hypothalamic center. The fall in the body temperature following intravenous infusion of vasopressin was not modified by neurohypophysectomy or total hypophysectomy, indicating that the effect is not mediated through hypophysial hormones or target gland hormones.

A possibility that the autonomic nervous function might be involved in the manifestation of the effect of vasopressin was ruled out by experiments
in which rats were treated with Dibenzylin or atropine to block the sympathetic or parasympathetic nervous activity respectively.

It is likely that the action of vasopressin is not central, but peripheral. Since vasopressin causes vasoconstriction of the skin, the loss of heat from the body surface will not be increased. The fall of the body temperature, in spite of the cutaneous vasoconstriction, may be resulted from the reduction of heat production. However, whether vasopressin directly suppresses the metabolic activity in the peripheral tissues or indirectly via cardiovascular disturbances, is not elucidated.

It was suggested by Ueno\textsuperscript{4} that vasopressin might play a role in the body temperature regulation in animals exposed to heat. The present experiments, however, indicated that vasopressin is of no significance in regulating body temperature in hot environment.

SUMMARY

1. In normal rats intraperitoneal as well as intravenous injections of Pitressin and synthetic lysine vasopressin caused a prompt fall in the rectal temperature. Pitocin and Syntocinon had no effect on it.
2. Intracarotid infusion of 8.5 per cent sodium chloride and 2M sucrose solutions resulted in a lowering of the rectal temperature in normal rats, but not in neurohypophysectomized ones. Intravenous infusion of the hypertonic solutions and intracarotid infusion of isotonic solutions did not cause any change in the rectal temperature.
3. Exposing neurohypophysectomized and totally hypophysectomized rats to a high ambient temperature of 40°C for 40 minutes resulted in a similar rise of the rectal temperature in extent and mode to that in normal ones. In rats with anterior hypothalamic lesions the rectal temperature rose to a higher level over 41°C on exposure to the same heat conditions.
4. Subcutaneous injection of Pitressin tannate in oil caused a prolonged fall in the rectal temperature, but it did not exhibit any suppressing effect on the elevation of rectal temperature either in normal or in neurohypophysectomized rats which were subjected to heat exposure.
5. No difference was observed between intracarotid and intravenous route of Pitressin administration in the extent and the time course of the fall in the rectal temperature.
6. The fall in the rectal temperature following intravenous infusion of Pitressin was not modified by electrolesions in the anterior hypothalamic area, neurohypophysectomy and total hypophysectomy.
7. Neither treatment with Dibenzylin nor atropine affected the body temperature lowering effect of Pitressin.
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REFERENCES


