tional role in the control of immunoglobulin precursors to CSF and to the circulatory system.

The obvious conclusion would be that hormone preparations are contaminated with serum IgG and albumin. Different hormones are expected to diffuse at different rates. Although this is true for reactions between whole molecules against specific countering antisera, we cannot ignore the fact that immunoreactions of similar determinants, originating within non-identical antigens, would show immune identity. This is clearly indicated in figure 4. Serum IgG identifies with determinants in the intraglandular colloid fractions and CSF as expected. However, when these fractions, and FSH are diffused against antiserum to whole bovine serum the major precipitate does not identify with either serum IgG or albumin.

These facts strongly support our contention that the production of intraglandular colloid, brought about by the cyclic breakdown of intermediate lobe cells, is related to the synthesis of hormones in the hypophysis. Furthermore, the accessability of this holocrine secretion to the venous circulation and to the cerebrospinal fluid suggests its implication in the transport of immunoreactive determinants.

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Effects of thyrotrophic-releasing hormone (TRH) on thermoregulation in the rat[1]

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Summary. At ambient temperatures (T_a) of both 8 and 22 °C, intraventricular administration of TRH (10–80 µg) produced a dose-dependent hypothermia in rats. The hypothermia was due to both decreased metabolic heat production and cutaneous vasodilatation. In contrast, at 30 °C T_a, TRH increased metabolic heat production (due to behavioral excitation) and led to hyperthermia.

Thyrotrophic-releasing hormone (TRH, pGlu-His-Pro NH_2) is found in, and is active on, neural processes throughout the brain[2–5]. In addition to its thyrotrophic action on the release of thyroid stimulating hormone (TSH), it has been shown that TRH in animals can reverse the CNS depression induced by barbiturates and alcohol[6,7]. Recently, Metcalf, Myers and Rice reported that intracranial injections of TRH produced hypothermia in cats but hyperthermia in rabbits[8–11]. In the present study, the effects of intraventricular injections of TRH on thermoregulatory outputs (including metabolic, respiratory and vasomotor activities as well as body temperatures) were assessed in the rat at various ambient temperatures (T_a).

Materials and methods. Adult male Sprague-Dawley rats weighing 250–300 g were used in all experiments. Measurements were obtained from conscious animals which were trained to sit quietly under minimal restraint in rat stocks. Between experiments the animals were housed individually in wire-mesh cages in a room of 25 ± 1.0 °C with a 12:12 h light-dark cycle. The animals were given free access to tap water and granular chicken feed. For intraventricular injection, ventricular cannulae were chronically implanted in the animals under anesthesia (sodium pentobarbital, 6 mg/100 g, i.p.). Implanatation of ventricular cannulae were carried out according to the DeGroot coordinates: AP, 7.0; Lat., 1.0; and Hor., 0.1 mm[12]. A 27-gauge Hamilton syringe needle was connected via PE-10 tubing to a 50-µl Hamilton syringe. During the surgery the correct positioning of each guide tube was verified by the rapid flow of saline or drug solutions into the lateral cerebral ventricle under gravity. At least 2 weeks were allowed for the animals to recover from the operation. All drug solutions were prepared in pyrogen-free glassware which was baked at 180 °C for 5 h before use. A 5-µl aliquot containing 10–80 µg TRH (Sigma) was administered into the lateral cerebral ventricle through a guide tube. Metabolic rate (M), respiratory evaporative heat loss (E_{res}) and vasomotor activities were measured in a small calorimeter[13–15]. M was calculated from the animal's oxygen consumption and expressed as W/kg b.wt. E_{res} was calculated by measuring the increase in water vapor content in the expired air. Evaporative heat loss expressed as W was calculated from evaporative water loss[13–15]. Rectal (T_r), foot skin (T_f) and tail skin (T_t) temperatures were measured using copper-constantan thermocouples. Rectal temperature was measured with a copper-constantan thermocouple enclosed in PE-200 tubing, sealed at one end, inserted 60 mm into the rectum. All measurements were taken once per 1 min throughout the experiments, each variable being measured as a direct current potential on a Hewlett-Packard digital voltmeter (DVM 3465) interfaced to an on-line CPU 9825 computer. Every min all temperatures, M and E_{res} were calculated instantaneously by the computer and relayed immediately back to the laboratory where they

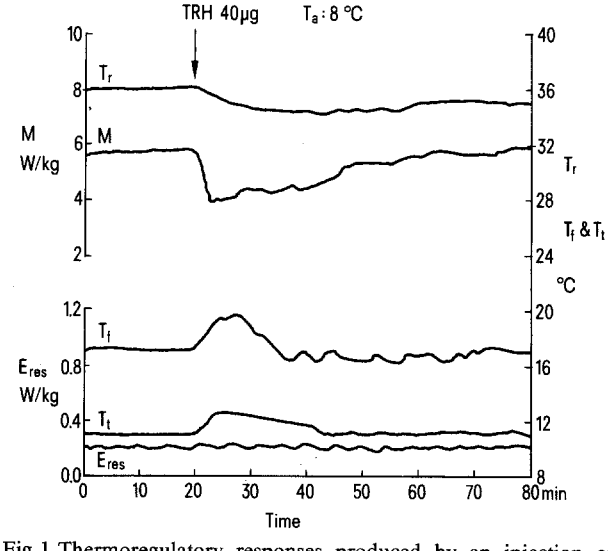

Fig. 1. Thermoregulatory responses produced by an injection of TRH into the lateral cerebral ventricle of a conscious rat at an ambient temperature of 8 °C.

were displayed by an on-line printer HP 9871. Animals were permitted 120 min to attain thermal balance before each drug injection. The maximal changes in T_r, T_f, T_t, M and E_{res} produced within a 80-min period after TRH injection were expressed as ΔT_r, ΔT_f, ΔT_t, ΔM and ΔE_{res}, respectively. The data were collected at 3 T_a of 8, 22 and 30 °C.

Results and discussion. Figure 1 shows that the administration of TRH into the lateral cerebral ventricle produced a dose-dependent hypothermia in rats at 8 °C T_a. The hypothermia developed almost immediately after the injection and T_r fell by 1.8±0.11 °C (for 40 µg TRH). The hypothermia was brought about by a decrease in M and an increase in cutaneous temperature (figure 1). There was no change in E_{res}. At 22 °C T_a, slight hyperthermia developed immediately after the injection and T_r increased by 0.5±0.07 °C (figure 2). However, the hyperthermia lasted for only 5 min and then was followed by a persistent hypothermia (1.4±0.09 °C for 40 µg TRH) (figure 2). The hyperthermia

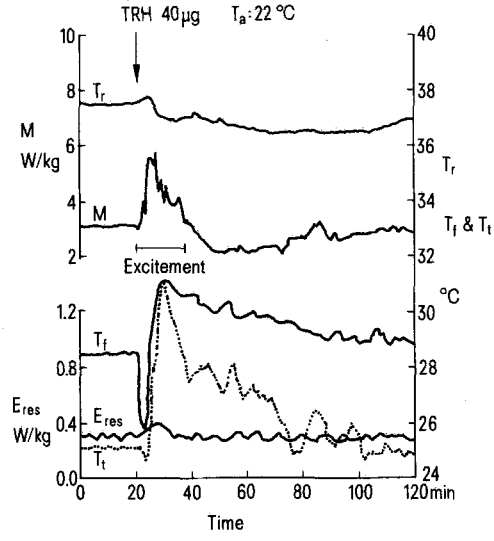

Fig. 2. Thermoregulatory responses produced by an injection of TRH into the lateral cerebral ventricle of a conscious rat at an ambient temperature of 22 °C.

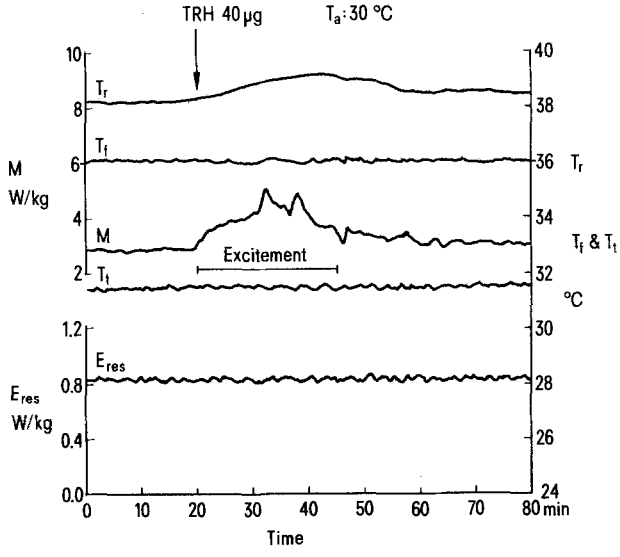

Fig. 3. Thermoregulatory responses produced by an injection of TRH into the lateral cerebral ventricle of a conscious rat at an ambient temperature of 30 °C.

was brought about mainly by an increase in M (due to behavioral excitation) while the hypothermia was due to both decreased metabolism and cutaneous vasodilatation. At 30 °C T_a, there was an increase in T_r (1.5±0.17 °C for 40 µg TRH) in response to TRH and the M was increased (due to behavioral excitation) by TRH at this T_a (figure 3). However, neither cutaneous temperature nor E_{res} was affected. The data indicate that the temperature effects induced by TRH were T_a-dependent. In general TRH inhibited heat production and facilitated heat loss which led to hypothermia in rats at 8 and 22 °C T_a, while at 30 °C T_a TRH facilitated heat production (due to behavioral excitation) and led to hyperthermia in rats.

In fact, current evidence is in favor of the view that central dopamine, serotonin and acetylcholine may play a hypothermic role in the rat. For example, it has been shown that intraventricular injections of dopamine[16] or apomorphine[13,17] and i.p. administration of gamma-hydroxybutyric acid[14] produced hypothermia in rats at both 8 and 22 °C T_a. Furthermore, activation of central serotonergic receptors with either the serotonin precursor[18], the inhibitors of serotonin re-uptake[19] or the serotonin itself[20,21] led to hypothermia in rats at the same T_a. Moreover, intracranial administration of acetylcholine or cholinomimetics produced hypothermia in rats at the same T_a[15,22-26]. The hypothermia in response to activation of either dopaminergic, serotonergic or cholinergic receptors was due to decreased heat production and (or) increased heat loss in rats. This is consistent with that of intraventricular administration of TRH demonstrated in the present study. It is not known whether the hypothermic effects of these substances are mediated by a common agent.

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