Cholecystokinin-induced hypothermia in the rat

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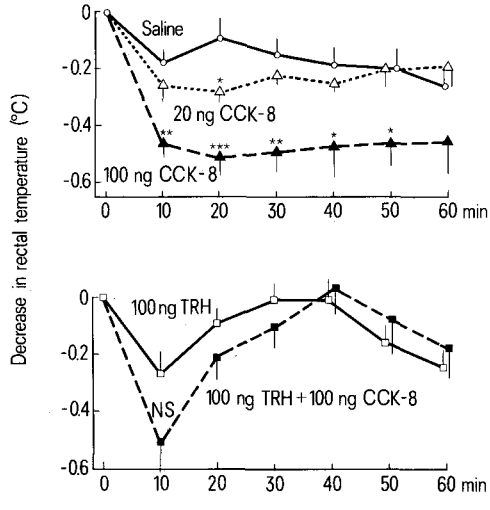
Summary. Cholecystokinin-octapeptide (CCK-8) was shown to cause hypothermia after intracerebroventricular administration in the rat, and the hypothermic effect of CCK-8 was antagonized by simultaneous injection of TRH.

The occurrence of cholecystokinin (CCK)-like peptides in the brain in amounts comparable to those found in the gastrointestinal tract has been shown by several investigators[1-4]. Further, its suppressive effect on the appetite[5], and its influence on the release of pituitary hormones such as gonadotropin, prolactin, growth hormone and thyrotropin, have also been reported[6,7]. We also found that a CCK preparation stimulates the pituitary-adrenal secretion[8]. In addition to these observations, the present study indicates that the peptide induces hypothermia when injected into the lateral ventricle of the rat.

Methods. Male Wistar rats, weighing approximately 250 g, were housed at a constant temperature of 25 ± 2 °C with a 12-h light and 12-h dark cycle, the light period starting at 07.00 h, and allowed access to rat biscuits (Oriental Yeast Co.) and water ad libitum. CCK preparations used in the present study were a) commercial CCK manufactured by Boots Co., the potency being expressed in terms of Harper unit, and b) synthetic C-terminal octapeptide of CCK (CCK-8, SQ 19844, batch No. NNO14NB) which was a gift from Mr S.J. Lucania of the Squibb Institute for Medical Research. Thyrotropin-releasing hormone (TRH) was purchased from Sigma Co. For intracerebroventricular (i.c.v.) injection, different doses of CCK-8 were made in a volume of 5 µl of 0.9% NaCl. The method of i.c.v. injection was described in detail in our previous paper[8]. Before the experiment the animals were accustomed to the injection and to the body temperature measurements. Core temperature was measured at a room temperature of 25 °C in the morning from 09.30 to 11.00 h by using a thermister at the depth of 5 cm from the anus.

Results. CCK (Boots Co.) caused a dose-dependent lowering of the body temperature. However, since the preparation was not pure, synthetic CCK-8 was used in the present study. Results are shown in the figure. Following i.c.v. injection of CCK-8 in a dose of 20 ng/rat a slight decrease of the body temperature was observed, while 100 ng of the peptide induced a marked and sustained hypothermia. In this experiment i.c.v. injection of TRH in a dose of 100 ng/rat resulted in a small drop of the rectal temperature 10 min after the injection, but thereafter the temperature was restored to the control level. When TRH was administered together with CCK-8, the hypothermic effect of the latter peptide was completely abolished. The difference 10 min after the combined injection (figure) was insignificant. This may be due to the large variation of individual results. It is also necessary to note here that the i.v. injection of CCK-8 in a dose of 20 µg/kg did not produce any change in the body temperature.



Decrease in rectal temperature of rats after i.c.v. injection of CCK-8 (upper figure) and effect of TRH on the hypothermic action of CCK-8 (lower figure). Number of rats was 10 in every experiment.

Discussion. Recently several reports have appeared on the thermoregulatory effect of hypothalamic neuropeptides. Vasoactive intestinal peptide was shown to produce hyperthermia[9], while neurotensin[10,11] and bombesin[12] were reported to cause hypothermia which was antagonized by TRH. As to the thermoregulatory action of TRH, controversial data have been presented; that is, it caused hypothermia in the cat[13] while causing hyperthermia in the rabbit[14]. In the present experiment, central administration of CCK was shown to produce a dose-related decrease in the body temperature, and this effect was antagonized by TRH. TRH itself may not have a potent action in inducing significant changes in the body temperature of the rat, but the tripeptide may play a role in the central thermoregulatory homeostatic mechanism. However, in order to clarify the role of CCK and TRH in the central thermoregulation, changes in the peptide content and/or metabolism should be examined in animals exposed to different environmental temperatures.

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