Thyrotropin-Releasing Hormone (TRH)-Induced Gastric Acid Secretion in Aging Rats

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There is much evidence indicating that the aging process involves an imbalance of the brain aminergic and peptidergic system (1-5). Dopamine receptors are reduced in aged rodents (6, 7). The concentration of TRH in the hypothalamus decreased in mid-life rats (8). Recently we have obtained evidence suggesting the interaction of dopamine receptor and thyrotropin-releasing hormone (TRH) for the central nervous system control of gastric acid secretion in the rat (9). These results suggest a possibility that the responses to TRH and/or dopamine receptors are changed in the gastric acid secretion of aged animals. In the present experiment to study the effects of aging, the activity of TRH on gastric acid secretion was examined during young- and mid-life in rats.

Female Wistar rats (derived from Hokuriku Lab. Co., Ltd.) were used after a 24 hr fast, but were allowed free access to water. Seven to eight weeks old rats weighed about 170 g, and 39-62 weeks old rats weighed about 300 g. The rat was anesthetized with urethane (1.25 g/kg, i.p.) and was placed in a stereotaxic apparatus. The gastric lumen was continuously perfused with saline solution through a gastric cannula, and the perfusate was titrated with NaOH solution using a fully automatic titrator system as previously described (10). TRH (Protein Res. Found.) dissolved in saline was administered intracerebroventricularly through a stainless steel cannula (0.35 mm, diam.) in a volume of 10 μl according to the technique of Noble et al. (11) with slight modification (10). Bethanechol dissolved in saline was given s.c. in a volume of 1 ml/kg. The total amount of acid secreted was expressed in terms of μeq HCl/90 min per animal and per kilogram body weight. The data indicate values in which the corresponding basal secretion before treatment was deducted from the acid output due to the treatment.

Intracerebroventricular TRH (5-20 μg/rat) stimulated gastric acid secretion in a dose-related manner in 7-8 weeks old and in 39-62 weeks old rats. However, the activity (μeq HCl/rat) of TRH (10 μg/rat) in 39-62 weeks old rats was weaker than that in 7-8 weeks old rats. Since there was a large difference in the body weights of 7-8 weeks old and 39-62 weeks old rats, the activity of TRH was compared in μeq HCl/kg. The low activity was also recognized in μeq HCl/kg. On the other hand, bethanechol (0.5 and 1 mg/kg, s.c.)-induced acid secretion (μeq HCl/rat and μeq HCl/kg) was not significantly different in 7-8 weeks old and 39-62 weeks old rats. Results are summarized in Table 1.

These results suggest that the sensitivity to TRH in the central nervous system decreases in 39-62 weeks, and the secretory function of parietal cells is not changed. In humans, TSH responsiveness to TRH diminishes significantly with increasing age (20-79 year old males) (12), although the function of the pituitary gland might merely be depressed in aged individuals. TRH is decreased in the hypothalamus, which is the control center of gastric acid secretion, of mid-life rats (8). Barnea et al. also described that the concentration of TRH decreased only slightly in the medial basal hypothalamus of aging female rats (13). It cannot be con-
cluded from our results whether the number of TRH receptors was decreased or the functions of the receptor and/or the overall CNS control mechanism of gastric acid secretion were lowered. Further studies are necessary for the examination of its precise mechanism and for the evaluation of the activity of TRH in aged rats.

References