Effects of cortisone and thyroxine on intestinal trehalase activity in infant mouse[1]

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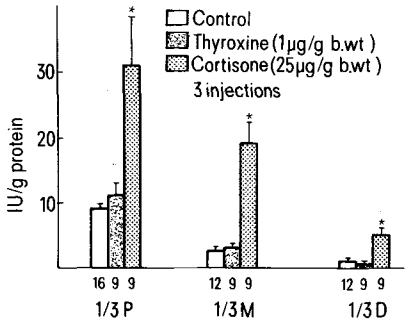
Summary. Cortisone acetate (25 µg/g b.wt/day) administration to 8-day-old suckling mice induces a premature increase of trehalase activity along the entire small intestine. On the other hand, thyroxine (1 µg/g b.wt/day) is unable to provoke a precocious increase of trehalase activity. Trehalase appears to be the only brush border membrane disaccharidase controlled solely by glucocorticoid hormones during the postnatal maturation of the intestine.

In the past years, considerable attention has been directed toward the hormonal control of maturation of the different brush border enzymes, namely maltase, sucrase, lactase, alkaline phosphatase and aminopeptidase. Numerous studies have clearly established the involvement of glucocorticoid hormones and thyroxine in the regulatory mechanism of enzymatic development[2-8]. Trehalase, which hydrolyzes trehalose to 2 glucose molecules, is also associated with the membrane of intestinal microvilli. This enzymatic activity is found in the intestinal mucosa of many mammals such as rat, mouse, guinea-pig, rabbit and cat[9], as well as in man[10]. Unfortunately, the hormonal control of the postnatal development of this particular disaccharidase is unknown. Recently, we have established the developmental pattern of trehalase activity in the different parts of the small intestine in suckling mice[11]. In order to find out whether trehalase responds to cortisone and thyroxine in the same manner as the other brush border enzymes, and more specifically as the other disaccharidases, we have studied the effects of repeated injections of these hormones on the activity of trehalase. The response of trehalase has been analyzed in the different parts of the small intestine in suckling mice.

Materials and methods. At 8 days of age, Swiss ICR mice were injected i.p. with cortisone acetate (Merck, Sharp and Dohme) suspension diluted in saline, or with DL-thyroxine (Sigma) dissolved in 0.005 N NaOH. Dosages were 25 µg cortisone or 1 µg thyroxine/g b.wt/day. Controls received equivalent amounts of the vehicles only. At the end of the experimental period, the intestines were removed immediately following decapitation, measured and cut into 3 equal parts. Each part was weighed and homogeneized in 99 vol. of ice-cold redistilled water. Trehalase, maltase and sucrase were assayed according to a modification by Lloyd and Whelan[12] of Dahlqvist's method[13], and proteins were determined according to Lowry et al.[14]. Enzymatic activities were expressed as µmoles of substrate hydrolyzed per min per g protein. Since disaccharidase activities observed in the different control groups did not show any difference, all data were combined and included in the figure and table as controls.



Influence of cortisone and thyroxine on trehalase activity. The hormonal treatments started at 8 days of age and the suckling mice received 1 injection/day for 3 days. Enzymatic activities are reported for proximal thirds (1/3 P), middle thirds (1/3 M), and distal thirds (1/3 D). Small numbers below each bar represent the number of intestines assayed for the controls and the cortisone and thyroxine-treated suckling mice. Differences between controls and cortisone-treated animals (1/3 P, $p < 0.005$; 1/3 M, $p < 0.0005$; 1/3 D, $p < 0.0025$).

Results and discussion. 1 injection of cortisone per day for 3 days induces a premature increase of trehalase activity in the small intestine of suckling mice (figure). The highest trehalase activity is noted in the proximal third and the lowest activity in the distal third. However, there is a 5-6-fold increase of activity in the middle and distal thirds as compared to a 3-fold increase in the proximal third. Galand and Forstner[4] have shown that trehalase activity can be detected in an homogenate of the whole small intestine of suckling rats and that repeated injections of cortisol acetate provoke an increase of trehalase activity. From the data reported in their paper, a 6.7-fold increase of trehalase activity can be calculated for the total small intestine. It appears that trehalase responds to glucocorticoid hormones in the same manner as sucrase, maltase, alkaline phosphatase and leucylnaphthylamidase in suckling rats and mice[2-5]. The maturation of the brush border enzyme activities during suckling and weaning period is not only controlled by glucocorticoid hormones but also by thyroxine. Indeed, Yeh and Moog[6,8] have shown that thyroidectomy affects the normal development of jejunal lactase, sucrase and maltase activities as well as alkaline phosphatase in suckling rats. They have also demonstrated that repeated injections of 1 µg/g b.wt/day of DL-thyroxine normalize the enzymatic development of the brush border in thyroidectomized suckling rats. Using intact suckling rats, Koldovsky et al.[15] have reported a precocious appearance of sucrase and an increase of maltase activity in the ileum, after repeated injections of 2 µg of thyroxine/g b.wt/day. Recently, Henning[7] has shown a premature increase of jejunal sucrase activity in intact suckling rats after administration of 1 µg/g b.wt/day of thyroxine during 3 days. In the present study, daily administration of thyroxine during 3 days at a dosage of 1 µg/g b.wt, induces a premature appearance of sucrase activity and an increase of maltase activity along the entire small intestine in infant mice (table). However, trehalase activity is not affected by thyroxine treatment (figure). Trehalase appears to be the only

Influence of thyroxine on maltase and sucrase activities in suckling mice

	Maltase		Sucrase	
	Controls	Treated	Controls	Treated
1/3 P	12.2±1.5 (16)*	67.0±6.8 (9)	0 (16)	2.2±0.5 (9)
1/3 M	16.8±1.3 (12)	39.3±5.3 (9)	0 (12)	0.8±0.2 (9)
1/3 D	29.8±2.1 (12)	64.2±5.2 (9)	0 (12)	0.6±0.2 (9)

Results are expressed as the mean of each group ± SEM. The hormonal treatment started at 8 days of age and the animals received 1 injection/day for 3 days. The animals were killed 24 h after the last injection. *Number of animals used in each group.

disaccharidase which does not respond to thyroxine during suckling period. These observations suggest that the hormonal control of the postnatal development of the different disaccharidases is not identical for all of them, trehalase being affected only by cortisone.

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Changes in efferent activities of the gastric vagus nerve by administration of glucose in the portal vein

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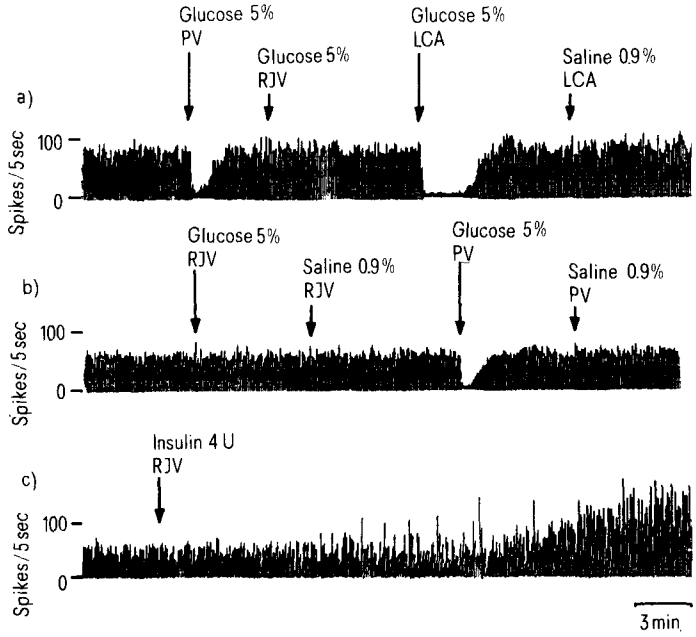
Summary. Injection of glucose in the portal vein, as well as in the left carotid artery, brought a transient decrease in efferent discharges of the gastric vagus nerve, whereas venous injection of regular insulin brought a gradual increase in the discharges.

It has been generally accepted that changes in the glucose concentration of the blood influence gastric secretion of acid which is attributed to the neural glucose sensitive mechanism in the central nervous areas[2-5]. However, behavioural and electrophysiological studies provide good evidence for the existence of neural glucose sensitive mechanism in the hepatoportal areas[6-8]. From these data, we speculated that there might be a close relationship between the neural glucose sensitive mechanism and secretion of gastric acid. Recently, we observed glucose injection in the portal vein that effected efferent activities of the gastric vagus nerve.

Material and methods. Experiments were made on 31 male rats weighing about 300 g under anesthesia with Pentobarbitone 45 mg/kg, i.p. Rectal temperature was kept at about 38 °C. The nerve innervating the stomach was dissected into a fine filament and covered with a mixture of vaseline and liquid paraffin. Discharges were taken from the cranial cut end of the nerve by means of silver electrode, amplified by an R-C coupled differential amplifier. The discharge was integrated after conversion of spikes to standard pulses through a window discriminator and was displayed as vertical deflections. 5% glucose and 0.9% saline solutions were injected through catheters placed in the portal vein, in the cardiac side of the right jugular vein and in the cranial side of the left carotid artery. Glucose was diluted with distilled water. The amount of the injection was fixed at 0.2 ml, so that no appreciable change in discharges was produced by control injection of the 0.9% saline.



a, b Effects of glucose injection into the portal vein, into the right jugular vein and into the left carotid artery upon the efferent activities of the gastric vagus nerve. PV: portal vein, RJV: right jugular vein, LCA: left carotid artery. *c* Effect of insulin administration i.v. upon the efferent discharges. Arrows indicate the time of injection.