

Induction of intestinal sucrase-isomaltase in suckling rats after hydrocortisone injections and substrate administration

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Summary. The *in vivo* action of hydrocortisone and specific substrates on intestinal enzyme adaptation has been studied after separation of enzymatic brush-border proteins by SDS electrophoresis. Daily hydrocortisone administration to neonatal rats between days 10 and 13 caused the protein band associated with saccharase-isomaltase activity to appear early. A similar result was obtained after saccharose was orally given to suckling rats between days 11 and 14. Determination of the specific activity of the mucosal homogenate showed that the substrate clearly had a more stimulating effect than hydrocortisone. The lactose diet also stimulated specific saccharase activity, but it mainly increased the specific activity of lactase and the corresponding protein band. Although we could not exclude some hormonal action induced by stress in our experimental conditions, the results suggested the determining role of disaccharide on the activation of the corresponding hydrolytic enzyme.

Introduction.

An hormonal role has been proposed in the change of disaccharidase patterns occurring at weaning in the rat intestine (appearance of sucrase and progressive decrease of lactase). Exogenous corticoids cause precocious appearance of sucrase in the rat intestine during the neonatal period (Doell and Kretchmer, 1962 ; Henning *et al.*, 1975). Also, the usual decline of lactase activity in rats can be prevented by thyroidectomy during the suckling period and restored by exogenous thyroxine administration (Yeh and Moog, 1974). On the other hand, a causal relationship between dietary changes at weaning and the appearance of active sucrase-isomaltase has not been clearly demonstrated (Rubino *et al.*, 1964), although a synergism between the dietary changes and the action of glucocorticoid hormones has been proposed (Lebenthal *et al.*, 1972).

In the present study, we have compared the effects of hydrocortisone injections and a high sucrose or lactose diet on intestinal disaccharidases in suckling rats.

Material and methods.

All experiments were performed with litters comprising at least 12 animals.

Hydrocortisone injections. — The litters were divided in half, one-half receiving 3 successive intraperitoneal injections of hydrocortisone sodium succinate (Solu-Cortef,

Upjohn Laboratories) at days 10 (1 mg/rat), 11 and 12 (0.5 mg/rat), and the remaining animals serving as controls.

Substrate administration. — Two groups (1 and 2) of 4 suckling rats each were removed from the mother at day 11 and were bottle-fed every 4 hrs until day 14. The basic diet (Raul *et al.*, 1978b) was supplemented with 13 p. 100 sucrose (Group 1) or 13 p. 100 lactose (Group 2). Group 3 included the rest of the litter and had normal access to maternal milk.

Separation and characterization of brush border enzymes. — Partial purification of intestinal brush border membranes and separation of brush border protein and enzyme assays were performed as described elsewhere (Raul *et al.*, 1978a).

Results.

In all experimental control groups, the protein patterns were similar and no sucrose-isomaltase was detected on the gels. The major protein band located in position 5 corresponded to lactase activity (fig. 1a).

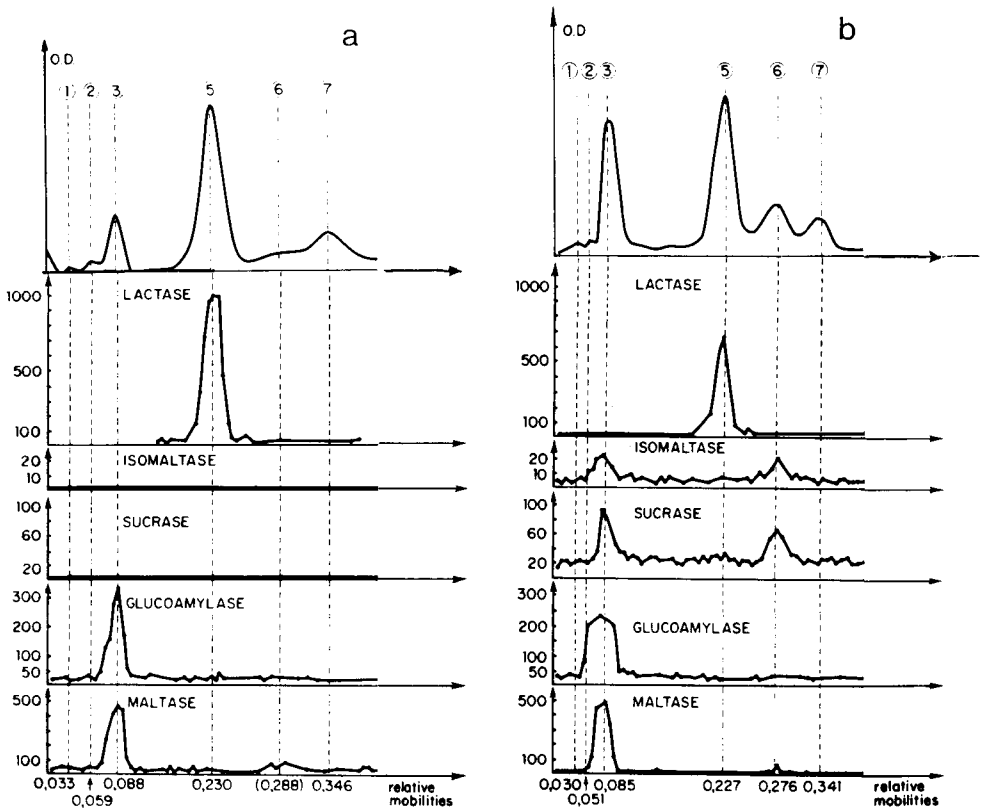


FIG. 1.

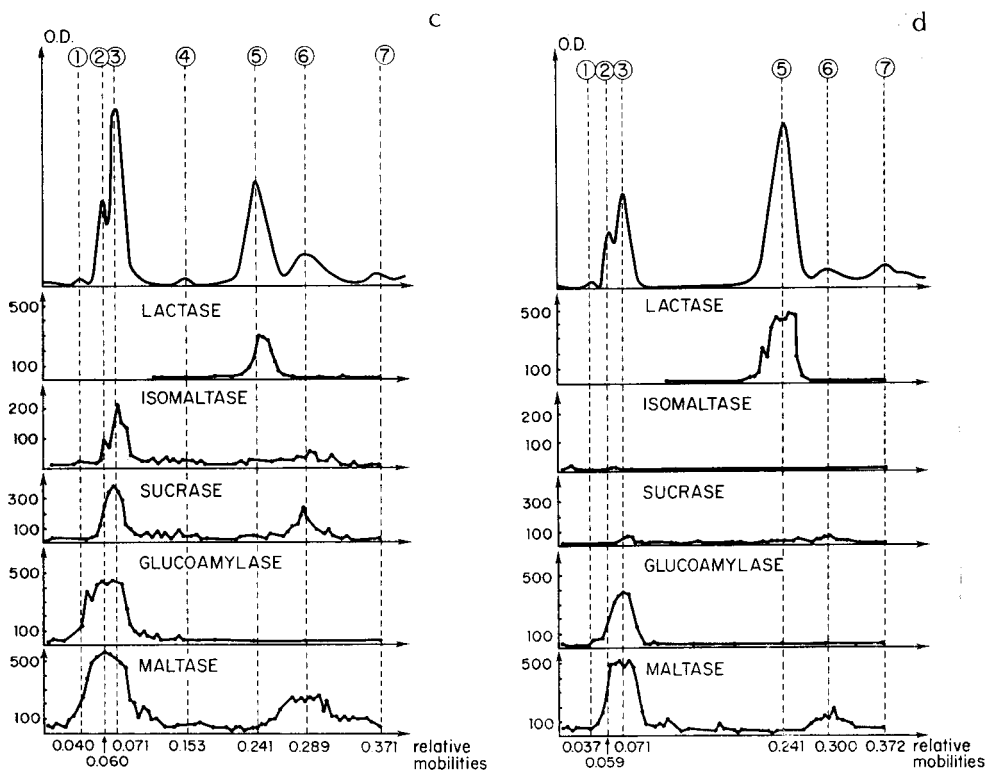


FIG. 1. — Representative protein and enzyme patterns of brush-border membranes after electrophoresis on 7.5 p. 100 polyacrylamide gels in the presence of sodium dodecylsulfate : a) 13-day control, b) after hydrocortisone injections, c) sucrose-fed animals, d) lactose-fed animals.

After hydrocortisone administration, the specific sucrase activities increased in the homogenate when compared to the controls, and remained unchanged for lactase (table 1). The protein and enzyme patterns were modified as follows : appearance of a clear protein band associated with sucrase-isomaltase activities (band 6), and increase of protein band 3 when compared to band 5 (lactase) with the simultaneous appearance of sucrase-isomaltase activities (fig. 1b).

TABLE 1

Specific activities (mU/mg protein) \pm SEM in the mucosal homogenates of control, hydrocortisone-treated and lactose or sucrose-fed rats

	Lactase	Sucrase
13-day controls.....	26.54 \pm 1.19	0
+ hydrocortisone.....	24.77 \pm 0.23	8.29 \pm 0.34
14-day controls.....	24.88 \pm 1.49	0.61 \pm 0.30
+ lactose.....	74.04 \pm 1.90	15.85 \pm 0.34
+ sucrose.....	18.83 \pm 1.96	54.26 \pm 2.19

The high sucrose diet administered to the animals of group 1 provoked a marked increase in the specific activity of sucrase and a slight decline in lactase activity in comparison to the controls (Group 3) (table 1). The protein and enzyme patterns of brush-border membranes isolated from the intestine of sucrose-fed animals (fig.1c) showed a sharp protein band (band 6) associated with sucrase-isomaltase and maltase activities. Furthermore protein band 3, which became the major protein band, was simultaneously associated with the appearance of sucrase-isomaltase activities and with a two fold increase of glucoamylase. The pattern was similar to that found in adult rats (Raul *et al.*, 1978a).

In the mucosal homogenates of lactose-fed animals the specific activities of both sucrase and lactase increased (table 1). The protein and enzyme patterns of brush-border membranes showed the following modifications in comparison to those of the basic controls (fig. 1 d) : protein band 5, the major protein band corresponding to lactase activity, was strikingly higher and a low but distinct protein band (band 6) appeared associated with a weak sucrase activity ; protein band 3 increased, associated with a two fold rise in glucoamylase activity and with the appearance of a low sucrase activity.

Discussion.

In our experimental system, gel electrophoresis revealed that hydrocortisone induced sucrase-isomaltase activity simultaneously with the appearance of a new protein band identical to that found in adults (Raul *et al.*, 1978). Thus, hydrocortisone initiated the precocious appearance of sucrase-isomaltase occurring only at weaning under normal conditions (Henning *et al.*, 1975). The electrophoretic patterns of brush-border proteins after sucrose or lactose feeding demonstrated an increase in the number of sucrase or lactase molecules which could result from the acceleration of enzyme synthesis. The most striking effect was obtained in the case of sucrose-fed rats since sucrase-isomaltase activities were absent at the beginning of force-feeding. Such an enzyme adaptation induced by the substrate was already obtained by Lifrak *et al.* (1976), who demonstrated that lactase synthesis could be increased in fetal rats by intra-amniotic injections of lactose. In our experimental conditions, a synergism between hormonal release (resulting from the basic diet or from stress) and the added disaccharide cannot be excluded. But the nature of the disaccharide present in the diet seemed to be a determinant in the specific activation of the corresponding disaccharidase.

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Résumé. L'action *in vivo* de l'hydrocortisone et de substrats spécifiques sur l'adaptation enzymatique intestinale a été étudiée après séparation électrophorétique, en présence de SDS, des protéines enzymatiques des bordures en brosse. L'administration quotidienne d'hydrocortisone à des jeunes rats entre 10 et 13 jours provoque l'apparition précoce de la bande protéique associée à l'activité saccharase-isomaltase. Un résultat similaire est obtenu après administration de saccharose par voie orale à des rats nourrissons entre 11 et 14 jours. La détermination de l'activité spécifique dans l'homogénat de muqueuse montre que le substrat exerce un effet stimulateur nettement plus élevé que l'hydrocorti-

sone. La diète au lactose est également capable de stimuler l'activité spécifique de la saccharase mais son principal effet s'exerce sur la lactase dont elle augmente et l'activité spécifique et la bande protéique correspondante. Bien qu'une certaine action hormonale induite par le « stress » ne puisse être exclue dans nos conditions expérimentales, ces résultats suggèrent un rôle prépondérant du disaccharide sur l'activation de l'enzyme hydrolytique correspondante.

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