

ADAPTATION OF THE EXOCRINE SECRETION OF RAT  
PANCREAS TO THE COMPOSITION OF THE DIET

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We reinvestigated last year (Desnuelle, Reboud and Ben Abdeljlil, 1962 ; Reboud, Ben Abdeljlil and Desnuelle, 1962) by more reliable techniques the early postulations of Grossman et al. (1942 43, 1944) according to which the composition of the diet induces statistically significant variations of the specific activities of several exocrine enzymes in rat pancreas. As a matter of fact, specific activities in fresh pancreas homogenates were found higher for amylase when the animals received a starch-rich diet, and higher for chymotrypsinogen when a casein-rich diet was given. Lipase behaved differently. It was low on the casein-rich diet and high on the others.

The case of amylase, chymotrypsinogen and other proteolytic enzymes of pancreas seems to represent a very interesting example of enzyme adaptation in mammals. It has now been investigated further by statistic and kinetic methods on rat pancreas homogenates and pancreatic juices.

In a first series of experiments, two groups of male, adult rats of the Wistar strain were fed ad libitum, respectively, on a starch-rich diet (starch, 75 % ; casein, 15 % ; corn oil, 4 % ; Osborne's salts, 4 % ; cellulose, 2 % by weight) and a casein-rich diet (starch, 20 % ; casein, 70 % ; oil, 4 % ; salts, 4 % ; cellulose, 2 %). Both diets were supplemented with the necessary vitamins. At the end of the experiments, all animals had an heal-

thy appearance and their weights were normal. On an average, the weight of pancreas and protein output per hour in pancreatic juice were the same in both groups.

After about 25 days, a Bollmann's fistula was placed on each animal. After an initial period of about 12-15 h., during which the secretion started again, bile was washed out of the cannula and the composition of the juice became constant, samples of pure pancreatic juice were collected in the cold for about 20 h. Samples showing turbidity or containing free trypsin activity were discarded. In the others (at least 10 for each group), specific activities of amylase, chymotrypsinogen and trypsinogen were determined by published techniques (Reboud et al., 1962). The average value for amylase activity was found to be about 2-3 times higher in the first group than in the second. The values for chymotrypsinogen and trypsinogen were, respectively, 2-3 times and 1.5-1.7 times higher in the second group than in the first. The differences were fully significant at the  $p \leq 0.01$  level.

The close parallelism between results obtained with homogenates and juices confirms in the first place that the diet exerts a significant influence on the composition of pancreas exocrine secretion. It further shows that the diet does not affect the relative rates of excretion of the enzymes into the juice, but actually governs the activity or number of enzyme molecules in pancreatic tissue and juice. Chromatography of rat juice in diethyl-amino-ethyl and carboxy-methyl cellulose columns demonstrates that the amount of amylase and chymotrypsinogen, rather than their activity, is modified by the diet (Marchis-Mouren, Paséro and Desnuelle, unpublished experiments).

The kinetic aspects of the variations were investigated in a second series of experiments when groups of rats fed for about a month on a given diet (starch-rich or casein-rich) were suddenly

fed on the other. After periods ranging from 1 to 30 days, the specific activities of amylase, chymotrypsinogen, trypsinogen and procarboxypeptidase B were determined in mixtures of five pancreas or three juices. Several pancreas or juices were used each time in order to lower the fluctuations around the average. Juices were mixed in proportions inversely proportional to their protein content. Fig. 1 shows the results of a typical experiment on juices. Results obtained with homogenates are quite similar.

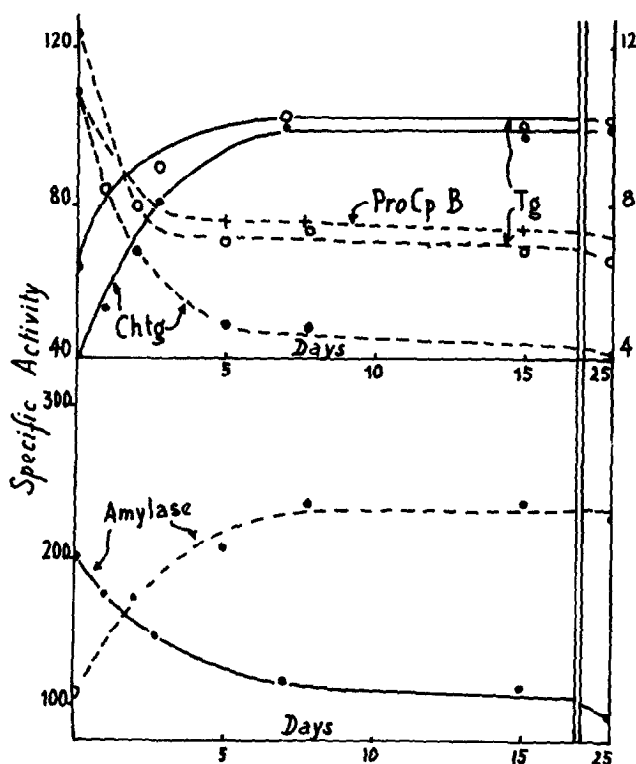


Fig. 1. Kinetics of enzyme adaptation in rat pancreas juice.

Specific activities ( $\mu$ -equivalents/min./mg total protein) of four enzymes (chymotrypsinogen (ChTg) and amylase, on the left ; procarboxypeptidase (Pro Cp B) and trypsinogen (Tg), on the right) are determined as a function of time in pancreatic juices of rats stabilized on a given diet (starch or casein-rich) and suddenly fed on the other at the start of the experiment. Solid and dashed lines indicate, respectively, the changes occurring when the starch-rich diet is replaced by the casein-rich or, on the contrary, when the casein-rich diet is replaced by the starch-rich.

The following comments can be made concerning Fig. 1 : (1) The adaptation to the new diet appears to start immediately or almost immediately. After one day, significant variations of the enzymatic levels are already detectable. (2) These variations occur for the main part within 3-5 days and become almost negligible after about 8 days. Similar kinetics have been found for the adaptation of urea cycle enzymes in rat liver when the protein content of the diet is varied (Schimke, 1962). (3) The new levels attained by the four pancreatic enzymes at the end of the adaptation period are quite stable for several weeks and reproducible within the limits of individual fluctuations and experimental errors. When experiments are performed in a given direction (for example, from a starch-rich to a casein-rich diet), the final levels reached by the four enzymes studied are very close to the initial levels found in the other direction.

Grossman et al. (1962) had pointed out that starch could be replaced by dextrose in a "balanced" diet without disturbing the enzymatic pattern which corresponds in pancreas to this kind of diet. We found that the kinetic curves obtained for amylase, chymotrypsinogen and trypsinogen by substituting to the casein-rich diet, either the starch-rich diet or a diet containing an equivalent amount of dextrose (75 % by weight) are very similar. This fact suggests that blood dextrose may be at least one of the factors determining the amount of amylase in pancreas and pancreatic juice.

Experiments designed for confirming this hypothesis and establishing a possible correlation between enzymatic levels in pancreas and rates of biosynthesis of the corresponding enzymes are in progress.

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