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Insulin, glucose and feeding behaviour in the rat

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Summary

Many cellular processes require energy. Fuel for producing this energy is taken up as food and reaches the cells via the blood, after digestion and absorption in the intestines. The most important fuels are glucose, free fatty acids and amino acids. The absorbed fuel can be used directly but can also be stored in the reserve tissues (liver and adipose tissue) from which the substances can be released when needed.

Mammals such as the subject of this research, the rat, maintain their body weight at a fairly constant level. The animal compensates its energy output by an equal input via food intake. This fact gives the impression that food intake is regulated. The aim of this research is to contribute to the clarification of the mechanism of that regulation.

It is clear that the animal uses satiety signals which inform its central nervous system about the fuel content of the body. According to the information received, the animal will decide to eat or to stop feeding. Several satiety signals are known (Chapter VII). It was repeatedly suggested that signals about blood sugar are important in this respect. It was shown that glucose availability (see p. 14) is correlated with the level of appetite in man. In this way the glucostatic theory was introduced, which predicts that if glucose availability is low, this will be a signal for the animal to eat. Low glucose availability can occur when either the glucose or the insulin content of the blood attains a low value, because for many cells the presence of insulin is needed for uptake and utilisation of glucose. If glucose availability is decreased by decreasing the blood sugar level by means of insulin injections, more food intake is

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performed. Competitive inhibition of intracellular utilisation of glucose with an analog of glucose, 2-deoxy-D-glucose, gives the same result. These facts show that under extreme circumstances a glucostatic regulation of food intake may be operating. The question remains, however, whether there is a glucostatic regulation under normal conditions. This is the major question of the present investigations.

Feeding of a carbohydrate rich meal causes a rise of the glucose level of the blood which is soon followed by a decrease to the same level as before the meal. The insulin level increases too, but then shows a gradual decrease attaining just before the next meal a value lower than any other value in the intermeal period. It is possible therefore that glucose availability is low before the meal, and that this acts as a signal for food intake (Chapter III). This idea has been tested in Chapter IV, in which by means of glucose infusions the blood sugar level and therefore also the insulin level is increased. However, no effect on the duration of the meal interval could be observed. In spite of the fact that glucose and insulin are relatively high, there is no delay of feeding behaviour. This result makes it unlikely that under normal ad libitum circumstances low glucose availability induces the start of a meal. It is very likely that other factors are more important.

Does high glucose availability furnish a stop signal for feeding behaviour? Infusion of glucose into the portal vein in dogs induces immediate cessation of feeding. These experiments were repeated in rats with the difference, that the glucose was administered in the general circulation (Chapter V). The glucose level in the general circulation, and therefore also in the portal vein, was much higher than ever measured after a meal (portal measurements). However, no cessation of the meal was observed. Therefore there is no proof available that in the rat high glucose availability gives a signal for stopping the meal under normal conditions (Chapter V).

Nevertheless it has been reported that under extreme conditions glucostatic governing of feeding behaviour can occur (see above). The question is raised where this glucose availability is measured. Since lesions in the ventromedial hypothalamus (VMH)

induce a clear desinhibition of feeding behaviour, this centre, called satiety centre, presumably is a link in the chain of mechanisms, which pass signals to the centres responsible for feeding behaviour. The glucose uptake of some cells of this centre seems to be dependent on insulin, whereas lesioning of these cells induces hyperphagia. It has been suggested that these cells are glucose receptors. To check this, local injections of a specific antibody against insulin were administered in the VMH to bind the insulin molecules at that place. Indeed feeding was stimulated (Chapter VI).

As a final conclusion (Chapter VII) it is stated that under normal circumstances the beginning and the end of a meal are dependent on glucostatic signals at most to minor extent. It is possible that the time pattern of the meals is governed by activation of receptors situated in the intestines. Feeding habits and interaction with other behaviour certainly play an important role in determining whether a meal will be started or stopped in the ad libitum condition. However, after theoretical analysis it is concluded that signals about caloric content of the body must play an essential role in caloric regulation. Especially the effects of a change in caloric content of the food argue for this.

After such a change gastrointestinal satiety signals cannot give reliable estimates how many calories are ingested. They must be calibrated anew. In this calibration glucose availability signals may play a role.

Samenvatti

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