Blood Glucose Levels in Portal and Peripheral Circulation and Their Relation to Food Intake in the Rat

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STRUBBE, J. H. AND A. B. STEFFENS. Blood glucose levels in portal and peripheral circulation and their relation to food intake in the rat. PHYSIOL. BEHAV. 19(2) 303-307, 1977. - Rats weighing about 450 g were provided with permanent catheters in the portal vein and the right auricle. This method allows blood sampling from the portal and peripheral circulation at the same moment in the nondisturbed unanesthetized rat. In the ad lib condition the portal glucose level was higher than that in the general circulation before, during, and after the meal. After a fast of 22 hr premeal portal vein levels were equal to those of the general circulation. During the meal the portal glucose levels rose to about 150 mg per 100 ml whereas those of the general circulation did not exceed 130 mg/100 ml. Experiments with glucose infusions systemically and intraportally show that, under conditions of mild deprivation, the level of glucose in the portal vein plays no or only a very minor role in the termination of feeding.

Blood glucose | Food intake | Portal vein

AFTER absorption from the intestines glucose is transported via superior and inferior pancreatico-duodenal vein, gastroduodenal vein, and several mesenteric veins to the main stream of the portal vein [2]. The blood of the portal vein flows through the liver where part of the glucose is absorbed. As the liver is the first organ through which the glucose flows it might play an important role in the regulation of food intake by signalling the amount of carbohydrate ingested. Evidence for such an involvement of the liver is presented by several authors [6, 7, 8, 9, 10, 11]. In particular, Russek demonstrated that portal infusion of large doses of glucose in the dog causes premature termination of an ongoing meal [7]. It therefore seems possible that termination of meals is under glucostatic control.

To put this hypothesis to a further experimental test an attempt was made to inhibit food intake in deprived rats by increasing the portal glucose concentration to high levels by means of continuous intracardial or intraportal infusion of glucose (Experiment 1). No inhibition was seen, but this alone was an insufficient basis for any conclusion as to the role of liver glucoreceptors in the control of food intake until it was shown that the glucose levels in the portal vein during infusion exceeded those during food intake (Experiment 2).

**METHOD**

**Animals and Maintenance**

Male Wistar rats were maintained in individual perspex chambers (25 x 25 x 30 cm) at a room temperature of 20°C. Lights were on from 6 a.m. till 6 p.m. Water was allowed ad lib at all times.

A standard diet providing 20% protein, 53.5% carbohydrate, 4.5% fat, and 22% water, with added minerals and vitamins was available ad lib except during food deprivation experiments. This diet was presented in the form of a bar which could slide easily through a dispensing tube attached to one of the walls of the cage. The bar could be removed from the dispenser after a meal and weighed without disturbing the animal. Practically no food was spilled. Experiments were made during day at about 10 a.m.

After surgery rats were not used until they proved to be influenced neither by the presence of an experimenter nor by his movements during blood sampling or infusion. It often took subjects a habituation period of about one week to reach this state. The experiments were performed while the animals remained in their living cages.

**Blood Sampling and Infusion Techniques**

To solve the problems stated in the introduction techniques are required that do not disturb the animals. Therefore cannulas were inserted into the heart of the animals through the jugular vein using the technique described by Steffens [12]. The swivel joint of Epstein and Teitelbaum [3] used by Steffens [12] was replaced by a very small swivel joint [13]. When systemic infusions were performed the animals were provided with a double heart catheter [12], allowing continuous intravenous infusions and blood sampling from the freely moving unanesthetized animals. However, the method of Steffens was somewhat...
modified. The infusion cannula ended 3 mm downstream from the tip of the sampling cannula in order to minimize the risk of contamination of the blood sample with the infusion fluid.

During repeated sampling (sample volume was 0.1 ml), stress on the rat due to loss of blood should be avoided. Therefore, fresh citrated blood taken from a donor rat by heart puncture and warmed to 39°C during 5 min, was transfused after each sample. During ad lib experiments donor blood of ad lib fed animals was used whereas during experiments with fasted animals blood of fasted animals was used.

**Portal Vein Cannulation**

Rats were anesthetized with ether. The hairs at the place of laparotomy, just right of the processus xiphoideus, were removed and the skin was sterilized with chlorhexidine 2%. A midline incision of about 1 1/2 to 2 cm was made. The caudal liver lobes were pushed in the caudal, and the rostral lobes in the rostral direction revealing the portal vein branches to the caudal liver lobes. The branch to the right lobe was taken for cannulation. The bile duct and the hepatic artery branch were carefully separated from the portal vein branch. The latter branch was cannulated in the manner described by Steffens [12] for heart cannulation but with a silicon catheter of ID 0.3 mm, OD 0.64 mm, 15 cm long. The tip of this cannula was pushed 1 cm in the caudal direction, so that it was situated between the liver and the superior pancreatic duodenal vein in the main stream of the portal vein. The cannula was drawn under the skin to the skull where it was attached as described by Steffens for the infusion cannula [12]. The cannula was filled with 50% polyvinyl pyrrolidone in a heparin solution of 500 U/ml.

Besides the portal cannula a heart catheter [12] was inserted. Sampling began 1 week after surgery. Blood was sampled in the day time about 4 hr after light went on.

**Chemical Determinations**

Blood glucose was measured with the ferri-cyanide method of Hoffman in a Technicon Autoanalyzer on samples of 0.05 ml whole blood.

**Experiment 1: Effect of Infusions on Feeding Behaviour**

In these experiments the rats, provided with the required sampling and infusion catheters, were fasted during 22 hr. After this fast the food was returned, and the rat began to eat almost at once. One min after the start of this meal, infusion of a 10% glucose solution was begun at a rate depending on the type of experiment, and continued during 30 min. In control experiments 0.2 ml/min saline was infused. Each rat was tested once in each condition used: the order in which conditions were presented was random. Meal size (g) and duration (min) were recorded.

**Experiment 1a, Intracardial infusion.** Five rats of about 350 g, provided with intracardial sampling and infusion catheters, were used. The rate of infusion was 0.083 or 0.2 ml/min (8.3 or 20 mg/min, respectively). In addition to the observations on feeding behaviour, blood samples for glucose determination were taken from the right auricle at 5, 10, 15, 20, and 25 min after meal onset.

**Experiment 1b, Intraportal infusion.** Six rats, body weight about 450 g, five of which had previously been used for Experiment 3, provided with intraportal as well as double intracardial catheters, were used. The glucose solution was infused through the intraportal catheter at a rate of 0.1 ml/min (10 mg/min). Only feeding behaviour was recorded.

**Experiment 2: Effects of Feeding on Blood Glucose Levels**

In this experiment the rats were always provided with intraportal and intracardial catheters. The influence of a meal starting at time zero, upon systemic and/or intraportal blood glucose concentrations were studied in rats previously deprived of food for 22 or 2 hr. The 2 hr deprivation was considered sufficiently similar to the ad lib condition, but has the advantage that it ensured that the rat would take a meal during the observation. In all cases the start of the meal is termed time 0. Blood samples from the right auricle and the portal vein were always drawn at the same moment.

**Experiment 2a, Ad lib 2 hr deprived.** Eight rats, body weight 400–450 g were used. Samples were taken at -20, -10, 0, 5, 10, 15, 20 min in all rats and in addition at 30, 40, 50, 60, 70, 80, 90 min in five animals.

**Experiment 2b, Intracardial infusion, 22 hr deprived.** Five animals, body weight 450 g, were used. Samples were taken in all animals at -20, -10, -5, 0, 5, 10, and 15 min and in four of the five also at 20, 25, 30, 40, 50, and 60 min.

For reasons to be discussed below, Experiment 3 was included.

**Experiment 3: Intracardial Glucose Infusion, 22 hr Deprived**

Five rats, body weight 450 g, were used. The rate of infusion was 0.2 ml/min (20 mg/min). Samples were taken from the general and portal circulation at 5, 10, 15, 20 and 25 min after meal onset.

**RESULTS**

**Experiment 1**

It can be seen from Tables 1 and 2 that neither meal duration nor meal size was significantly influenced by the glucose infusions administered as compared with saline infusion, irrespective of whether the glucose was infused intracardially or intraportally.

**Experiment 2**

**Blood glucose concentrations.** The influence of intracardial glucose infusion on the time course of glucose levels in general circulation during a meal is presented in Fig. 1. For the sake of comparison, the time course of GC glucose levels during a meal with saline infusion is included in this figure. Even at the lower infusion rate (8.3 mg/min) GC glucose rises far higher than during the saline infusion, but especially at the higher infusion rate (20 mg/min) excessive hyperglycaemia is rapidly induced in the GC.

**Experiment 2a**

a. Blood glucose concentrations. As regards the portal circulation (PC) it should be emphasized that portal glucose levels are higher than in the GC before ($p<0.05$) and during ($p<0.05$) the meal, and also during most of the period after the meal (Fig. 2).

b. Blood glucose concentrations. The main difference
TABLE 1
EFFECT OF INTRACARDIAL GLUCOSE INFUSION ON FEEDING BEHAVIOR

<table>
<thead>
<tr>
<th></th>
<th>Meal Duration (min)</th>
<th>Meal Size (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline infusion 0.2 ml/min</td>
<td>21 ± 0.9</td>
<td>6.4 ± 0.4</td>
</tr>
<tr>
<td>Glucose infusion 8.3 mg/min</td>
<td>19.8 ± 1.6</td>
<td>5.7 ± 0.7</td>
</tr>
<tr>
<td>Glucose infusion 20 mg/min</td>
<td>19.4 ± 2.3</td>
<td>6.7 ± 1.1</td>
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</tbody>
</table>

TABLE 2
EFFECT OF INTRAPORTAL GLUCOSE INFUSION ON FEEDING BEHAVIOR

<table>
<thead>
<tr>
<th></th>
<th>Meal Duration (min)</th>
<th>Meal Size (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose infusion (10 mg/min)</td>
<td>20.1 ± 2.7</td>
<td>8.4 ± 1.3</td>
</tr>
<tr>
<td>Saline infusion (0.1 ml/min)</td>
<td>19.7 ± 1.6</td>
<td>8.2 ± 0.9</td>
</tr>
</tbody>
</table>

FIG. 1. Effect of intracardial glucose infusion on the glucose levels in the general circulation, during meal intake after a fast of 22 hr. For meal size and duration, see Table 1. • glucose 20 mg/min, 0.2 ml/min o glucose 8.3 mg/min, 0.083 ml/min • saline 0.9% NaCl, 0.2 ml/min.

with Experiment 2a is that before the meal glucose levels in PC and GC are the same. After meal onset, PC levels are significantly (p<0.05) higher than those in GC at 10, 15, 20, 25, and 30 min (Fig. 3).

Experiment 3
Figure 4 shows that, as was to be expected, upon intracardial glucose infusion in 22 hr deprived rats the glucose level in the PC, which before the meal did not differ from that in the GC, rises significantly (p<0.05) higher than systemic concentration at 15 and 25 min. At sample times 5, 10, and 20 min the PC glucose level was not significantly higher (0.05<p<0.01).

DISCUSSION
Russek showed that deprived (22 hr) dogs, after return-
refute this possibility [1] then, portal glucose either in the
portal glucose levels sufficiently.

and PC glucose levels after infusion of glucose in the GC
in agreement with those of Michaelis [4]. The latter findings were
these levels rose even higher than those of the general

FIG. 4. Effect of glucose infusion on the glucose levels in portal vein
- - - general circulation o - - after a fast of 22 hr.

ing the food, stopped eating as soon as large loads of

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