EFFECT OF DAMAGE TO THE VENTROMEDIAL HYPOTHALAMIC NUCLEI ON THE STATE OF THE PANCREATIC ISLETS IN RATS ON A RESTRICTED DIET

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Experiments on albino rats with electrolytic injury to the ventromedial hypothalamic nuclei (VMHN) showed that adiposity of the animals and hyperplasia of the pancreatic islet tissue when the diet was unrestricted are due not only to hyperphagia and the resulting increased load on the β-cells. In animals with damaged VMHN, kept on a strictly measured and restricted diet, the accumulation of fat also was increased and the volume of the insular tissue was increased as a result of direct stimulation of the pancreatic islets. However, these changes were less marked than in animals on an unrestricted diet. Depending on the conditions both these factors evidently can combine in different ways and lead in some cases to exhaustion of the β-cells and to the development of diabetes.

Electrolytic injury to the ventromedial hypothalamic nuclei (VMHN) leads to hyperphagia and adiposity [1-8] and these, in turn, are considered to throw a load on the insular apparatus [1-3, 10, 18]. In recent years the adiposity has been attributed to the increased secretion of insulin taking place directly after injury to VMHN and independently of an excessive intake of food, rather than to the hyperphagia [9, 13, 15, 16]. However, the state of the insular apparatus in animals with damaged VMHN and on a restricted diet (eliminating the role of hyperphagia) has not been investigated.

The investigation described below was carried out to fill this gap.

EXPERIMENTAL METHOD

Experiments were carried out on 22 adult female Wistar rats. Bilateral injury to VMHN was produced in 16 of the rats in a stereotaxic apparatus with a direct current of 2 mA acting for 15 sec. When the animals began to develop hyperphagia 2-5 days after the operation they were put on to a balanced diet, 100 g of which contained 47 g potato starch, 41 g casein, 12 g rendered beef fat, corn oil, and fish oil with the addition of 4 g of a mixture of mineral salts and a polyvitamin complex [17, 19]. The same diet was given to 6 intact (control) animals. Each rat received this diet in a daily amount equivalent to 44 calories and water ad lib. The blood sugar was determined by the Hagedorn–Jensen method, sugar in the urine by Benedict's method, and the total fat content in the cadaver was estimated [12] after the end of the experiments. The localization of the injury was established with the aid of De Groot's atlas [11] in serial sections through the hypothalamus stained with 0.05% azure. To demonstrate insulin deposited on the β-cells, sections through the pancreas were stained with aldehyde-fuchsin [7] and pseodoisocyanin [20]. The state of the insular tissue was judged from the number of islets in 10 mm^2 of the gland, the mean number of cells per islet, the percentages of α and β cells in the islets, and the β/α ratio. The relative percentage of insular tissue in the pancreas was determined in serial sections through the whole organ at intervals of 600 μ. The outlines of the islets and sections were drawn with a drawing apparatus and measured with a planimeter.

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TABLE 1. Effect of Injury to VMHN on Pancreatic Islets in Rats

Group of animals	Number of animals	Fat (in % of weight of cadaver)	Number of islets (per 10 mm² pancreatic tissue)	Quantity of insular tissue (in % of total weight of pancreas)	Number of cells in islet	Percent of β-cells in islet	Ratio β/α
Control	2	5,4±0,9	11,0±0,07	0,71±0,06	68,6±4,1	76,8±4,5	3,3±0,4
With damage to VMHN	8	14,5±0,6	14,6±0,7	1,02±0,04	109,7±7,7	81,4±7,0	4,5±0,3
P		<0,05	<0,01	<0,001	<0,01	<0,02	>0,2

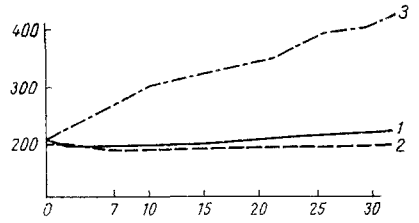

Fig. 1. Changes in weight of control and experimental animals depending on conditions of feeding: 1) experimental animals on restricted diet; 2) control animals on restricted diet; 3) experimental animals on unrestricted diet. Abscissa, time (in days); ordinate, weight (in g).

EXPERIMENTAL RESULTS

The experimental animals ate their ration of food greedily within 20-30 min whereas the control animals ate theirs much more slowly. During the first 7 days the weight of the rats of both groups fell a little (Fig. 1); later the weight of the control rats remained at a constant level whereas in animals with injury to VMHN it increased slightly. The increase in weight in the animals undergoing the operation was relatively small but statistically significant ($P < 0.05$), but a much greater increase in weight was observed in the animals with injury to VMHN which received food ad lib (Fig. 1).

Repeated determination of the blood sugar in the animals of the control and experimental groups revealed no significant differences (108 ± 6.1 and 101 ± 2.6 mg %, respectively; $P > 0.2$).

On the 32nd-35th day of the experiment 8 of the experimental and 3 of the control rats were killed, and the remaining animals were put onto a unrestricted diet. During the next 50 days the weight of the rats with injury to VMHN, which ate much more food, increased considerably, reaching 452 ± 3.7 g.

Investigation of the brain sections showed that the VMHN in the experimental animals were completely destroyed. The fat content in the cadaver of the experimental animals was significantly higher than in the controls (Table 1). These animals had thus accumulated fat even though after injury to VMHN the rats had been kept on a strictly restricted diet.

Microscopic investigation of sections through the pancreas showed an increase in the number of islets in the experimental animals compared with the controls. The total content of insular tissue and the number of β-cells producing insulin also were increased in the experimental rats.

No appreciable difference in the staining properties of the sections through the pancreas from the control and experimental animals was discovered, from which it could be deduced that there was no significant difference in the insulin content in the insular tissue.

The increased accumulation of fat, the hyperplasia of the islets, and the increase in volume of insular tissue cannot therefore be attributed entirely to the hyperphagia arising after damage to VMHN. In that case the injury to VMHN evidently directly stimulated the internal secretory function of the pancreas. This conclusion conforms with results of experiments by other workers [9, 14, 15]. Meanwhile, the difference in the degree of adiposity in the experimental animals receiving an unrestricted or a restricted diet suggests that in the presence of marked hyperphagia the direct stimulation of the insular apparatus as a result of injury to the hypothalamic nuclei could not be the only cause of the deposition of fat. Consequently, the factor of overeating plays an essential role in adiposity and, correspondingly, in the overstraining of the insular apparatus of the pancreas after injury to VMHN.

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