THE PART PLAYED BY THE CAROTID CHEMORECEPTORS IN REGULATING THE BLOOD SUGAR LEVEL

V. F. Markelova and A. M. Ugolev

Laboratory of General Physiology (Director, Active Member AMN SSSR V. N. Chernigovskii)
Institute of Normal and Pathological Physiology (Director, Active Member
AMN SSSR V. N. Chernigovskii) AMN SSSR, Moscow
(Presented by Active Member AMN SSSR V. N. Chernigovskii)
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The blood glucose level plays an important part in the regulation of appetite [1, 6, 7, 10]. According to the "glucostatic" theory [8, 9] hypoglycemia excites the glucoreceptor cells of the hypothalamus, which leads to stimulation of the appetite. When glucose enters the bloodstream, the glucoreceptor cells are inhibited, and the desire for food is reduced. Many facts support this viewpoint. When glucose is injected into the blood stream of dogs, the rhythmical gastric hunger contractions are reduced [6], and in man the sensation of hunger is diminished. However, some authors have been able to find no relation between the peripheral blood glucose level and the response to food [12]. V. A. Tychinin and A. M. Lukaneva [4] consider that insulin does not increase, but rather reduces, the drive to obtain food. Nevertheless, most investigators attribute regulation of the activity of the feeding center to variations in the blood glucose level.

Evidently, the effect of the glucose level in the blood is conveyed not only to the glucoreceptor cells of the hypothalamus, but also to peripheral sensory endings. Quite recently it has been found that removal of the carotid bodies in rats causes a marked reduction in appetite [5]. It is thought that the response of the carotid bodies to variations in glucose level is still more important in maintaining the constancy of the internal medium. V. A. Tychinin [3] and A. I. Karaev [1], using acute preparations, have shown that perfusing the sinocarotid zone with hyperglycemic solutions causes a reduction in the peripheral blood glucose level. If the receptors are perfused with a hypoglycemic solution, there is then a marked increase in the blood sugar level. The responses so produced are certainly reflex, because they are eliminated by treating the receptors with novocain. Both the hyper- and hypoglycemia induced by stimulation of the chemoreceptors of the carotid bodies are developed gradually, so that the process may be described as having a considerable inertia. It must, however, be noticed that all Tychinin and Karaev's results were obtained in acute experiments in which extremely high or very low concentrations of glucose were used. Therefore, the sensitivity of the chemoreceptors of the carotid zone to variations in blood sugar and their importance in the maintenance of a constant blood sugar level require to be further tested while the animal is in the normal conscious condition.

The object of the present investigation has been to determine in such an animal the part played by the carotid bodies in maintaining the blood sugar at a constant level in face of glucose or insulin injections.

METHOD

The work was carried out on 16 male rabbits weighing 3,400-4,000 g. In all of them, the blood sugar curve was determined after injecting 1 ml per kg of 40% glucose, and in seven the curve was taken after injecting 0.03 milliequivalents of insulin per kg. Both the insulin and the glucose were injected into a superficial ear vein. After studying the initial response of all the rabbits except two, which were controls, the carotid bodies were removed. The operation was performed under barbiturate anesthesia. The approach was made through a median incision. The carotid bodies were cauterized with a hot needle [2].

All the animals recovered uneventfully. Experiments were resumed 3-5 days after the operation, and were continued for 3-4 weeks. The results of the experiments on the animals in which the carotid bodies had been removed were compared with those obtained on unoperated animals before the operation. Blood was collected from an ear vein before the injection of glucose and insulin, while the animal was in a fasting condition, and 10, 30, 60, and 120 minutes after the injections had been given. Sugar was estimated by Nelson's arsenomolybdate method [12].

RESULTS

In the nonoperated animals, ten minutes after giving the glucose injection, the blood sugar level rose to 240-280 mg%. However, the hyperglycemia was not long maintained, and as a rule, after 50 minutes, it returned to the original level. In most experiments, by the end of the second hour, the blood sugar level was somewhat below the starting point, as measured before the glucose injection. The experiment was repeated on

TABLE 1. Glycemic Response to an Intravenous Injection of Glucose in Rabbits after Removal of the Carotid Bodies

Number of rabbit	Before or after operation	Blood sugar (mg %)				
		Before glucose injection	Time after glucose injection (in minutes)			
			10	30	60	120
1	Before	93	240	180	90	105
	After	150	312	200	147	155
2	Before	122	235	190	155	113
	After	95	317	215	120	100
3	Before	140	277	180	136	145
	After	102	305	200	150	140
4	Before	137	250	—	177	145
	After	145	295	—	160	140
5	Before	130	238	—	135	100
	After	125	305	160	107	110
6	Before	135	238	170	130	105
	After	128	322	175	140	105

each animal 3-5 times, and we never noticed any regular changes in the blood sugar curve which distinguished the repeat injections from the first one. The reason was, perhaps, that the experiments took place under conditions in which it was not possible for a conditioned reflex to glucose injections to be developed.

It can be seen from Table 1 that removal of the carotid bodies caused no regular changes in the blood sugar levels obtaining before the glucose injections. In some animals, there was some tendency toward an increase (rabbit no. 1), and in others to a decrease (rabbits nos. 2 and 3).

In most rabbits, the levels before and after the operation were nearly the same. We found no essential differences in the shape of the blood sugar curves of the intact and the operated group at considerable times after the glucose injection. Thus, 60 minutes after the glucose injection, the blood sugar had returned to its original level. However, removal of the carotid bodies has a marked influence on the initial phase of the response to the increased sugar load, so that at first there is a considerable increase in the blood sugar.

The results obtained were very consistent, and indicated that the carotid sinuses are not one of the principal means of glucose homeostasis. If the receptors of the sinocarotid zone consistently exerted a control over blood sugar level, then it would be expected that their removal would result in a persistent hyper- or hypoglycemia. Despite the interesting observations of V. A. Tychinin [4] and A. I. Karaev [1], and other workers, which were made on acute preparations, and which give reason to suppose that such a control was exerted, we have been unable to confirm them under the conditions of our own experiments. Evidently, the carotid chemoreceptors play only a small part even in mediating such comparatively slow processes as the gradual return to normal of the blood sugar level after an injection. However, their effect is clearly seen in restricting sharp fluctuations in the first few minutes after a glucose injection has been given.

Both before and after the operation, in all the experimental animals, intravenous injection of insulin produced a fairly standard reaction, which began after ten minutes with some reduction in the blood sugar level—though in some of the experiments there was no change at this time. The greatest hypoglycemic reaction occurred after 30 minutes. At the end of the first hour, the blood sugar was at approximately the same level as after 30 minutes, though in most of the experiments it was somewhat higher. After 2 hours there was still a considerable increase, though it was returning to normal, and in none of the experiments had it actually reached its original value. The fact that intravenous injection of saline caused no noticeable changes in blood sugar level showed that the experimental conditions and the process of performing the injections did not by themselves exert any effect.

After 4-5 experiments, which enabled the typical response of each animal to insulin to be determined, the operations were performed. The experiments were repeated 3-5 days after removal of the carotid bodies. Just as in the first set of experiments, no definite changes in the glucose concentrations were observed in blood removed before the insulin injection. This result once more demonstrates the fact that the blood sugar level is regulated by some other mechanism.

It can be seen from Table 2 that removal of the carotid bodies has practically no effect on the shape of the blood sugar curve after definite amounts of insulin have been injected. This effect is due both to the extent of the hypoglycemia which developed, and to the nature of the response to insulin.

Thus, in experiments in chronic preparations, as has been described in detail above, it was not possible to detect any influence of the carotid bodies on the hypoglycemic response induced by intravenously injected insulin.

TABLE 2. Glycemic Response to Intravenous Injection of Insulin in Rabbits after Removal of Carotid Bodies

Number of rabbit	Before or after operation	Blood sugar (in mg%)				
		Before insulin injection	Time after injecting insulin (in minutes)			
			10	30	60	120
1	Before	129	116	73	71	85
	After	150	130	62	67	113
2	Before	142	103	72	80	108
	After	135	118	75	62	92
3	Before	136	129	60	62	90
	After	127	124	62	57	106
4	Before	149	149	60	69	102
	After	150	155	99	87	130
5	Before	144	123	69	78	115
	After	160	160	84	81	113
6	Before	120	92	60	76	97
	After	124	94	75	74	85

The primary purpose of the work reported here was to determine the part played by the carotid chemoreceptors in maintaining the blood sugar level constant. Our results differ very definitely from those obtained by other authors in acute preparations.

Actually, the changes in the peripheral blood sugar produced by perfusion of the carotid zone with hyper- or hypoglycemic solutions were so stable that it was thought that signals from the carotid chemoreceptors are largely responsible for determining blood sugar levels. However, this interpretation is at variance with the fact that removal of the carotid bodies in the chronic preparation has practically no effect on the "spontaneous" blood sugar level. If such changes were absent only long after the operation, there might be some talk of compensation. However, it seems to us most unlikely that any such compensation occurs, because by the third day after the operation, the blood sugar level was the same as that occurring during the preoperative period. Experiments in which the responses of animals to intravenous sugar or insulin injections were measured both before and after removal of the carotid bodies showed that the operation had no effect on insulin hypoglycemia or on any of the changes caused by a glucose injection. The observed changes occurred only very shortly (10 minutes) after the injection. It may therefore be supposed that the carotid chemoreceptors which play such an important part in maintaining the constancy of the internal medium are concerned only to a very restricted extent in controlling rapid blood sugar concentration changes.

SUMMARY

Experiments on rabbits were performed in chronic preparations, in which the glycemic responses to intravenous injections of sugar or insulin were measured before and after removal of the carotid bodies. It was found that the operation influenced neither the degree of insulin hypoglycemia nor the response to intravenous glucose injections. The only changes observed occurred 10 minutes after its administration. This result suggests that the carotid chemoreceptors, which play an important part in maintaining the constancy of the internal environment, may also control large sudden changes in blood sugar concentration.

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