MECHANISMS OF THE EFFECT OF INSULIN HYPOGLYCEMIA ON MOVEMENTS OF THE LARGE INTESTINE

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UDC 616.153.455.04-02:615.357.37]
-092:9-07:616.345-009.1

Movements of the pyloric part of the stomach and the proximal part of the large intestine were recorded in dogs by inserting balloons into them and recording the pressures. Subcutaneous injection of insulin (0.5 unit/kg) was shown to increase movements of the pyloric part of the stomach and of the proximal part of the large intestine; the latent period of the motor response in the large intestine was shorter than in the pyloric part of the stomach. Division of the right vagus nerve in the chest abolished the effect of insulin hypoglycemia in stimulating movements in the proximal part of the large intestine. Additional intrathoracic division of the left vagus nerve abolished the motor response of the pyloric portion. The parasympathetic innervation of the proximal part of the large intestine is supplied entirely by fibers running in the right supradiaphragmatic trunk of the vagus nerve.

The action of insulin hypoglycemia in stimulating movements of the proximal part of the large intestine in dogs was first described in 1929 [13]. Investigations were published later which confirmed [4,6,10] or rejected this effect [12, 14]. There is no unanimity among investigators who have observed stimulation of the contractions of the large intestine by insulin regarding the mechanisms of this effect. Some workers [13] consider that the vagus nerves and n. erigentis are concerned in its mechanism while others [6, 14] deny that the vagus nerves play any role. The authors have investigated the effect of insulin hypoglycemia on movements of the large intestine in order to shed light on its mechanisms.

EXPERIMENTAL METHOD

Experiments were carried out on four dogs with fistulas in the proximal part of the large intestine (10-40 cm distally to the ileocecal sphincter). Two dogs also had fistulas of the pyloric part of the stomach. Movements of the pyloric part and of the rectum were recorded as the contractions of a balloon inserted into their lumen. The volume of air inflating the balloons did not exceed 4 ml. The experiments began 18 h after the animals had fed. During the first 90-120 min the background movements were recorded, after which the animals received a subcutaneous injection of insulin in a dose of 0.5 unit/kg and the movements of the stomach and large intestine were recorded for 5-7 h longer. This dose of insulin, according to previous investigations [3], induces a definite motor response of the stomach in 100% of cases. In some experiments, besides recording the movements, the blood sugar was determined every 30 min by the Hagedorn-Jensen method.

A two-stage intrathoracic vagotomy, dividing the trunk of the nerve, was performed on two dogs: the right vagus nerve was divided in the first stage and the left vagus nerve in the next.

The numerical results were subjected to statistical analysis [7].

Department of the Physiology of Digestion, Institute of Physiology, Kiev University. (Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Sirotin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 76, No. 9, pp. 12-15, September, 1973. Original article submitted December 13, 1972.

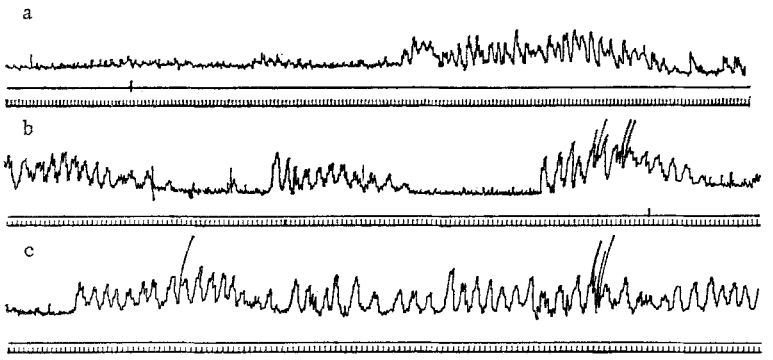

Fig. 1. Motor response of proximal part of large intestine to insulin: in the resting state (a), continuation (b), and during a period of work (c). Here and in Figs. 2 and 3, from top to bottom: record of movements of proximal part of the large intestine, marker of time of insulin injection in a dose of 0.5 unit/kg, time marker: each interval represents 15 sec.

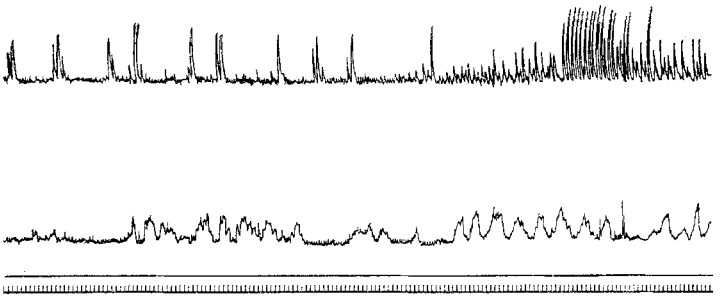

Fig. 2. Beginning of motor response to insulin in pyloric part of stomach (top curve) and in proximal part of large intestine (bottom curve).

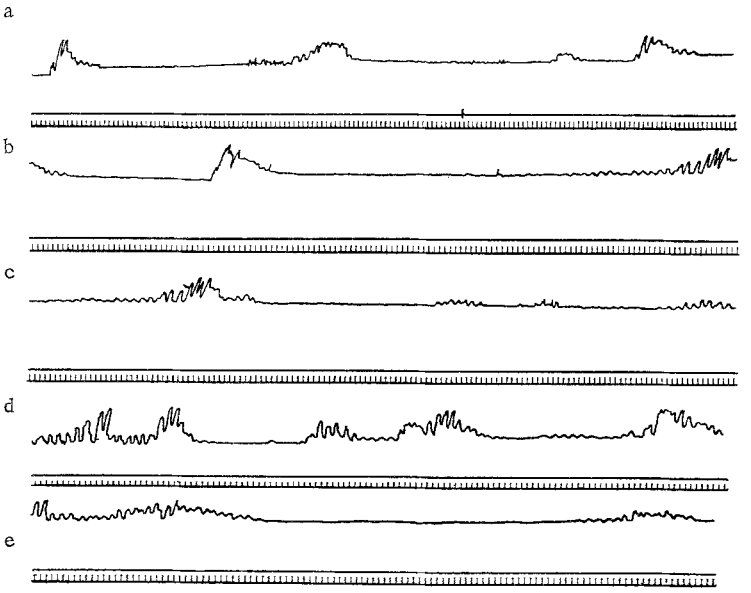

Fig. 3. Motor response of proximal part of large intestine after injection of insulin (a), continuation (b,c) in dogs after division of the right vagus nerve in the chest, and movements of pyloric portion of stomach under the influence of insulin in bilaterally vagotomized dog (d and e).

EXPERIMENTAL RESULTS AND DISCUSSION

Injection of insulin into the dogs in 100% of tests stimulated movements of the large intestine, as shown by an increase in the amplitude of the contractions, a decrease or the complete disappearance of the pauses between the typical series of contractions for the large intestine, and an increase in tone. If the original motor activity was strong, only the pauses disappeared between the series of contractions, so that the intestinal movement became continuous (Fig. 1). The latent period of this response of the large intestine to insulin was 24.4 ± 2.4 min and its duration 93.3 ± 10.06 min. If the movements were recorded simultaneously at two points in the large intestine 20-30 cm apart, as a rule the motor response began simultaneously at these points.

Comparison of the motor responses of the large intestine and pyloric portion of the stomach showed that the latent period of responses of the small intestine was about half as long as that of the stomach (Fig. 2). The degree of lowering of the blood sugar at which the motor response began was much less for the large intestine (70-80 mg%) than for the pyloric portion of the stomach (55-60 mg%). Division of the right vagus nerve in all the experiments completely abolished the increased motor activity of the distal part of the large intestine produced by insulin hypoglycemia (Fig. 3a,b,c). The motor response of the pyloric portion remained unchanged. In 30% of the experiments, during the appearance of a contractile effect in the stomach, weak inhibition of movements of the large intestine was observed. Subsequent division of the left vagus nerve completely abolished the motor response of the pyloric portion to insulin (Fig. 3d, e). Moreover, in the completely vagotomized dogs a distinct and profound inhibition of movements of the large intestine and a simultaneous slight depression of the contractile activity of the pyloric portion of the stomach occurred as a rule 72.8 ± 10.8 min after the injection of insulin. The duration of total adynamia of the large intestine in some cases amounted to 150 min.

These results confirm the fact, discovered earlier, that insulin hypoglycemia stimulates the motor function of the large intestine [5, 7, 11, 15]. Attention is directed to the fact that the latent period of the motor response in the large intestine was much shorter than in the stomach despite the fact that efferent impulses are transmitted to both organs along the vagus nerves. The threshold of the excitatory action of hypoglycemia on central structures concerned with the regulation of movements of the large intestine is evidently lower than that for structures controlling movements of the stomach. In the modern view [5, 9, 11] insulin hypoglycemia causes excitation of the glucoreceptive zones of the hypothalamus, which have a stimulating action on the organs of the digestive tract through the parasympathetic nervous system and, in particular, through the vagus nerves. Characteristically the motor responses of the small and large intestine to direct stimulation of the hypothalamic structures through implanted electrodes are also much less than the contractile effects of the stomach [1, 2].

The present experiments show that the stimulant effect of insulin hypoglycemia on movements of the large intestine is mediated only through the right vagus nerve, which is evidently the sole source of parasympathetic innervation of the proximal part of the large intestine. It must be assumed that fibers reaching the large intestine leave the right vagus nerve in the branch leading to the solar plexus. The discrepancy between these observations and the results of other authors [4], who showed that the insulin motor response of the large intestine is effected through the sacral outflow of the parasympathetic nervous system and not through the vagus nerves, can probably be explained by the fact that in the present experiments the motor activity was recorded in the proximal, and not the distal (sigmoid colon) half of the large intestine.

The hypothesis that the excitatory effect of insulin hypoglycemia reaches the large intestine through the vagus nerves and n. erigentis [13] can thus evidently be considered proven.

The question of the mechanisms of the inhibitory effect of insulin hypoglycemia on movements of the large intestine in vagotomized dogs is not yet clearly understood although it may be postulated that the effect is produced through the sympathetic nervous system, which also participates in the overall response of the body to hypoglycemia [8].

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