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Hepatic glucose signals vagally modulate the cyclicity of gastric motility in rats

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Abstract. The cyclicity and intensity of gastric motility were examined following glucose injection into the portal vein with an intragastric balloon in anesthetized rats. Enhanced gastric motility caused by insulin administration was influenced by 4 mM glucose (25 µl) injected into the portal vein; glucose provoked a shift in the cyclicity power spectrum without any change in intensity. The peak power spectrum shifted from 4.0–5.0 cpm to 2.0–3.0 cpm. Hepatic branch vagotomy abolished the response.

The results suggest that glucose signals in the hepatic vagal branch modulate the cyclicity of gastric motility.
Key words. Gastric motility; cyclical movement; gastric pressure; glucose; portal vein; hepatic vagal nerve.

Gastric motility has been shown to consist of constrictive cyclicity and intensity when recorded with an intragastric balloon, and such motility is partially controlled by the vagal nerve through a change in central nervous activity[1,2]. The hepatic vagal nerve has also been shown to affect gastric motility; glucose injected into the portal vein vagally suppresses enhanced intragastric pressure associated with insulin-hypoglycemia[3,4]. However, the relation of the hepatic vagal nerve to the cyclical movement of the stomach has not yet been examined. Recently we observed that hepatic glucose signals selectively modulate the cyclicity of gastric motility.

Method

Ten male Wistar rats weighing about 250 g were used. The animals were fed on a standard diet with free access to tap water, but were deprived of food for 22 h before the experiment. On the day of the experiment, rats anesthetized with pentobarbital sodium (45 mg/kg, i.p.) were bilaterally adrenalectomized about 30 min before the experiment[4].

The evaluation of gastric motility was performed by the method described previously[3]. A polyethylene tube with a small balloon on the end of it was introduced into the stomach through the esophagus and filled with water at 36.0 °C. The intragastric pressure was measured with a strain-gauge transducer and adjusted to 0.78–0.98 kPa at the onset of recording. The data were stored on magnetic tape, and were reproduced as necessary.

Insulin (Actrapid, 42 µg/kg/h) was administered to stimulate basal gastric motility, and experiments were carried out 40–100 min after the insulin administration. Anal temperature was kept about 36 °C with a heating lamp.

D-glucose (glucose) solution kept at 36 °C was injected into the portal vein. 25 µl was infused each time with an infusion pump through a catheter introduced into the portal vein, and was completed in 10 s. Blood (20 µl) was drawn through the same catheter for glucose estimation and the plasma concentration of glucose was measured[4]. The glucose concentrations (mean ± SE) before and 4 min after portal glucose injection were 3.21 ± 0.03 and 3.22 ± 0.05 mM (n = 10), respectively. The glucose injection did not affect the glucose concentration in the blood.

The power spectrum and intensity area of motility were obtained by the autoregressive power spectrum analysis[5,6], and an averaged power spectrum was also obtained. The intensity area was given as the area of deviation from the basal line. Statistical significance between values was assessed by *t*-test.

Results and discussion

When intensity areas were calculated between 0.5 and 5.0 cpm, the areas (mean ± SE) of motility obtained during 3 min before and 3 min after portal injection of 4 mM glucose (25 µl) were 24.1 ± 0.6 and 23.8 ± 0.8 (n = 10), and there was no significant difference between the values.

When gastric movement was expressed as a power spectrum for 3 min before portal glucose injection, there was a characteristic power spectrum in the motility, showing a peak between 4.0 and 5.0 cpm. This peak was shifted to between 2.0 and 3.0 cpm by portal glucose injection (fig.). When power spectra with intensity above 2 dB and cpm above 1.0 were picked up, the peak levels of cpm (mean ± SE) before and after glucose injection were 4.1 ± 0.1 and 2.6 ± 0.1 cpm (n = 10), and a significant difference ($p < 0.05$) between the two values was obtained. This response to portal glucose injection was not reproduced after hepatic branch vagotomy. These findings are partially consistent with the view that a mechanism receptive to glucose in the portal vein participates in the vagal control of gastric motility[3,4].

Gastric motility consists of cyclicity and intensity[1,2]. In the present study, a significant shift in the power spec-

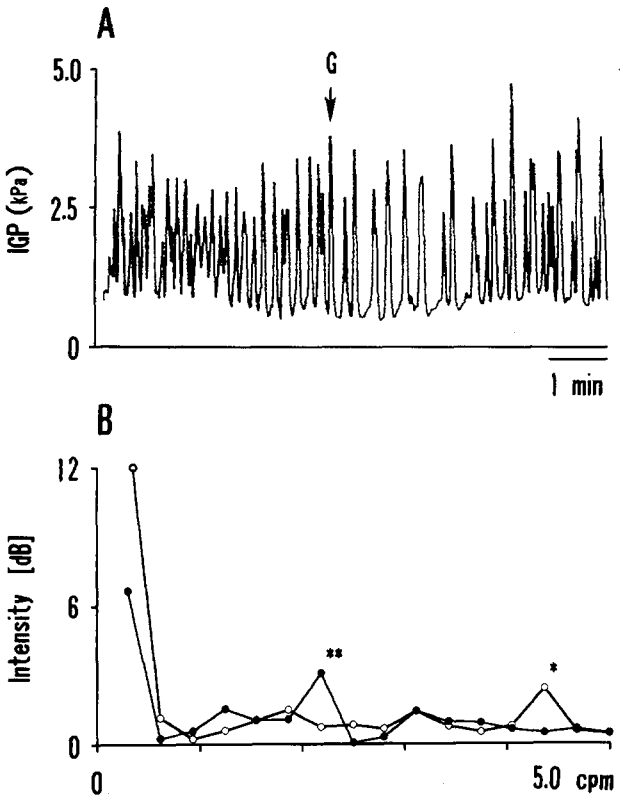

Figure. *A* A recording showing changes in intragastric pressure (IGP) caused by portal injection of glucose. 4 mM glucose (25 µl) was injected. The arrow indicates the time of injection (G). *B* Peak power spectrum for motility obtained during 3 min before (○, *) and 3 min after (●, **) 4 mM glucose injection is shown. Values are means (n = 10).

trum of gastric motility was seen without any change in intensity area when 4 mM glucose solution (25 µl) was injected into the portal vein. Considering these results together with the report indicating that glucose less than 5 mM (25 µl) injected into the portal vein failed to change the intragastric pressure[4], it is possible that the hepatic glucose signal has an action that specifically regulates the cyclicity of gastric motility.

Pharmacological doses of glucose (20 mM, 25 µl) injected into the portal vein provoked a reduction in intragastric pressure[4]. But in this study a shift in the power spectrum for motility was induced even when a physiological concentration of glucose was injected into the portal vein. This could be interpreted as meaning that afferent glucose signals from the portal vein[7] can regulate the cyclicity of gastric motility in a physiological range.

Glucose solution injected into the nucleus of the vagus nerve depressed intragastric pressure[8], and almost the same response in the power spectrum of gastric motility was obtained in rats when 4 mM glucose was injected into the vagus nucleus of the medulla oblongata (unpublished data, Ohtake and Sakaguchi). The nucleus of the tractus solitarius received afferent signals from the portal vein areas[9], and there is a fiber connection between the two nuclei[10]. Hepatic glucose signals may therefore modulate gastric motility by means of these medullary nuclei.

Because tonic activation of descending pathways has been shown to alter the rhythmicity of the movement-pattern generating circuitry in the spinal cord in cats[11], there might be a similar mechanism in the observed gastric response. The mechanism by which presumed tonic sensory feedback signals from the hepatic vagal nerve affect the rhythmicity of gastric motility remains to be elucidated.

These observations led us to suggest that glucose signals in the hepatic vagal nerve modulate the cyclicity of gastric motility.

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