Gastric branch vagotomy and gastric emptying during and after intragastric infusion of glucose

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Kaplan, John M., William H. Siemers, Ulrika Smedh, Gary J. Schwartz, and Harvey J. Grill. Gastric branch vagotomy and gastric emptying during and after intragastric infusion of glucose. Am. J. Physiol. 273 (Regulatory Integrative Comp. Physiol. 42): R1786–R1792, 1997.—The effect of gastric branch vagotomy (GVX) on the gastric emptying of glucose was evaluated during two phases of emptying control: as the stomach fills and in the postload period. GVX and control rats received a series of intragastric glucose infusions (1.0 ml/min) through indwelling gastric fistulas. In experiment 1, gastric samples were withdrawn either immediately after the offset of 9- or 18-min infusions of 12.5% glucose or at various times up to 36 min postinfusion. In experiment 2, samples were withdrawn immediately or 30 min after termination of 12-min infusions of 12.5% or 25% glucose. After gastric fill, glucose solute emptying rate was stable over time, not influenced by concentration doubling, and, surprisingly, not affected by GVX. During gastric fill, solute emptying rate doubled with concentration in both GVX and control rats. For each concentration, however, glucose emptied during fill at almost twice the rate in GVX compared with control rats. This accelerated emptying of glucose during fill in GVX rats is consistent with a gastric vagal contribution to inhibitory mechanisms (e.g., receptive relaxation) that operate as the stomach fills under normal conditions. The absence of a GVX effect on emptying after fill suggests either that gastric branch vagal efferents play little role in feedback inhibitory control of glucose emptying during normal conditions or that other systems compensate for the function previously served by vagal gastric branch efferents. Further work is required to address the possible role of the gastric vagus in feedback control of gastric emptying when nutritive fluids other than glucose are delivered.

GASTRIC EMPTYING OF FLUIDS is accelerated after section of the gastric branch of the vagus nerve (26, 32), suggesting a disruption of mechanisms that operate normally to restrain emptying. Studies of vagal influences on gastric tone and gastric pressure, principal determinants of fluid emptying (18), suggest that gastric branch vagotomy (GVX) would interfere with several emptying-inhibitory reflexes. For example, gastric branch afferents and efferents contribute to the receptive relaxation of the stomach during stomach fill (1, 11), and gastric vagal efferents appear to represent the gastromotor limb of a relaxation response to volume distension of the duodenum (10). In addition, gastric vagal efferents, through their influence on gastric tone, may contribute significantly to the feedback inhibition of fluid emptying that attends chemical stimulation of the intestinal receptors by emptied nutrients (4, 5, 23). Attribution of the accelerated fluid emptying observed after GVX to disruption of one or more of these mechanisms is challenging because other, nonvagal (splanchnic, hormonal), systems may also influence gastric tone in response to mechanical or chemical stimulation of the gastrointestinal tract and may, in addition, compensate to some extent for the loss of gastric vagal control after GVX. We show here that attention to the time course of gastric emptying in GVX and control rats can offer useful clues about which gastromotor functions underlie the rapid emptying that follows GVX.

In the present experiments, we explore the effects of GVX on two distinct phases of gastric emptying control: the period during which the stomach is filling and the interval that begins when gastric fill ceases. Previous work indicated that different mechanisms govern gastric emptying during vs. after controlled intragastric infusions of glucose (17). After gastric fill, solute emptying rate was stable over time and, moreover, was not influenced by variation in glucose concentration (6.25–25%). This result conformed well to the principle of feedback regulatory control (19–21), according to which solute emptying rate is held within relatively narrow limits as a function of inhibitory signals that arise from nutrient stimulation of intestinal receptors. A different set of rules appeared to govern glucose emptying while the stomach fills. The rate of glucose solute emptying was considerably (4–9 times) higher during than after gastric fill. The higher rate of emptying persisted throughout the gastric fill period regardless of its duration. Also, in contrast to the postfill emptying profile, the rate of solute emptying during gastric fill varied broadly with changes in glucose concentration. It was suggested (17) on the basis of these results that emptying during fill was less sensitive to the chemical nature of the infusate than to mechanical factors associated with the dynamic increase in stomach volume.

From this perspective, we reasoned that an analysis of the effects of gastric vagotomy that distinguishes the two phases of gastric emptying control may highlight the different functions normally served by this branch of the vagus nerve. For example, accelerated gastric emptying in the postinfusion period may emphasize the contribution of gastric efferents to feedback inhibition driven by chemical stimulation of the intestine. An effect of gastric vagotomy on emptying during fill may emphasize the role of gastric efferents in the inhibitory

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response to mechanical stimulation of the stomach or intestine.

Data reported by Schwartz et al. (26) indicate that the effect of GVX, in fact, is not uniform over time. In that study, different nutrients were delivered in 5-ml boluses, with the gastric contents sampled at various intervals after gastric loading. For glucose and other macronutrients, the increased emptying observed in GVX relative to control rats was fully expressed by the time of the first gastric sample, which was taken 5 min after bolus delivery. Interestingly, for the remainder of the observation period (5- to 40-min postload samples), emptying appeared to be somewhat slower in GVX than in control rats. In light of our perspective on differential controls of emptying during and after gastric fill, the results of Schwartz et al. (26) might suggest that the influence of the gastric vagus is most profound in close temporal relation to the fill period and that the gastric vagus contributes little to the feedback control of gastric emptying after the gastric load has been delivered. However, 1) the 5-min sample taken by Schwartz et al. (26) does not permit a distinction between amounts emptied during vs. immediately after the brief period of bolus delivery. 2) Only a fraction (=1 ml in most cases) of the 5-ml bolus initially delivered to GVX rats remained in the stomach by the time of the first gastric sample. The interpretation of the GVX effect in the postload period therefore depends on whether very low gastric volumes affect subsequent emptying (or emptying rate). 3) Finally, one can question in general terms whether results obtained with bolus-delivery paradigms are indicative of gastric emptying control when fluid is delivered to the stomach at rates more typical of normal ingestion.

In the present study, GVX and control rats received a series of intragastric infusions of glucose solution (12.5 and 25%) delivered at a rate (1.0 ml/min) within the range of ingestion rates observed in the rat licking the same fluid from a drinking spout (15). Gastric samples were withdrawn either immediately after infusion offset, to assess the average rate of emptying during fill, or at various points after infusion offset. The results obtained demonstrate that the effect of GVX on glucose emptying is marked but entirely limited to the period of gastric fill.

METHODS

Subjects

Male Sprague-Dawley rats (Charles River, MA) weighing 180–274 g at the time of surgery were used. They were maintained on a 12:12-h light-dark schedule in a temperature-controlled vivarium and were tested between 5 and 8 h after lights on.

Maintenance

Each day, rats were given access to a drinking spout containing 40 ml milk diet (1:1 Borden's sweetened condensed milk:water, with 1 ml Polyvisol added per 500 ml diet).

Surgery

All rats underwent gastric fistula implantation surgery under ketamine-xylazine anesthesia. A gastric cannula (5 mm ID) was fixed to the ventral forestomach according to the method of Weingarten and Powley (31) and was exteriorized through an abdominal puncture. Further surgical details appear in Refs. 16 and 17. GVX rats received gastric fistula and transection of the dorsal and ventral branches of the gastric vagus nerve in the same surgical procedure. The GVX procedure was as described in Schwartz et al. (26). Briefly, dorsal and ventral branches of the gastric vagus were each isolated by blunt dissection and were ligated with silk suture at two positions at least 1 cm apart. The isolated nerve sections were then cauterized between the ligatures.

Verification of Gastric Vagal Section

The completeness of the gastric vagotomy was verified by postmortem analysis with the use of fluorescence histochemistry as described in Berthoud et al. (6). Five days before death, rats were deprived of food overnight and on the next day were injected intraperitoneally with 1 ml saline containing 1.25 mg fluoroagold. Rats were killed with an overdose of barbiturate. After intracardiac perfusion with 4% Formalin solution, brains were removed and placed in 10–15% Formalin-sucrose. Coronal sections through the dorsal motor nucleus of the vagus nerve (DMN) were evaluated for fluorescent labeling of cells reflecting the retrograde transport of fluorogold. A gastric vagotomy was judged successful by the absence of such labeling in the central subregion of the DMN on each side. Rats were rejected from the study if the histochemical appearance of the DMN departed significantly from this profile (e.g., with labeling absent on one side but present on the other or with the label-free region including the expected location of motor neurons serving the celiac or hepatic vagal branches).

Procedure

One hour before each daily gastric emptying test, the gastric fistula was opened and the contents of the stomach were removed by gentle lavage with isotonic saline. The fistula was then closed, and the rats were placed into a holding cage where they remained before being placed in the rectangular Plexiglas test chamber.

Stimulus delivery. Five minutes before intragastric infusion, the rubber infusion tube (3.2 mm ID) was filled with the test fluid (12.5 or 25% glucose) and press fitted into an insert that was then threaded into the gastric fistula. The tube was clamped at the mouth of the fistula until the beginning of the infusion. All intragastric infusions were delivered at a rate of 1.0 ml/min.

Withdrawal and analysis of gastric sample. Immediately after the termination of the intragastric infusion, the tube was again clamped and then cut, leaving ~1 cm of tubing to accommodate insertion of the 20-ml syringe used to withdraw the contents of the stomach. The gastric contents were then either removed immediately or were removed after a scheduled delay. After removal of the primary sample, return from a 10-ml gastric flush was also collected. The amount of glucose (in g) remaining in the stomach was taken as the product of the measured volume of the gastric contents and the glucose concentration of the withdrawn sample, measured via the glucose oxidase method (Beckman II glucose analyzer). The amount of glucose solute (in g) emptied from the stomach (glucose infused -- gastric glucose) was taken as the principal dependent measure for statistical comparisons. Infusate volume (in ml) emptied / glucose emptied (g) ×
[100/infusate concentration (g/ml)] was also used as a dependent measure in experiment 2.

Rats received two to four habituation training sessions, beginning 7 to 11 days after surgery. During each habituation session, gastric contents were withdrawn immediately after termination of a 12-min intragastric infusion of 12.5% glucose.

Experimental Design

Experiment 1. Beginning 8–16 days after surgery, GVX (n = 7) and intact (n = 5) rats received a series of five once-daily intragastric infusions (12.5% glucose, 1.0 ml/min) across which infusion duration and sample latency were varied. Testing began 8–16 days after surgery and was completed 16–21 days after surgery. Three 18-min infusions were delivered (2.25 g glucose delivered), with the gastric contents withdrawn either immediately or 18 or 36 min after infusion offset. Two 9-min infusions were delivered, with gastric samples taken either immediately or 9 min after infusion offset. The five tests were delivered in counterbalanced order across rats. The results of the 18-min infusion conditions were analyzed by a two-way [group (GVX/intact) x sample latency (0, 18, and 36 min)] analysis of variance (ANOVA). The 9-min infusion results were analyzed by a separate two-way [group x sample latency (0 and 9 min)] ANOVA.

Experiment 2. Beginning 14–16 days after surgery, GVX (n = 7) and intact (n = 6) rats received a series of four once-daily 12-min intragastric infusions delivered at 1.0 ml/min. For two infusions, 12.5% glucose was infused (1.5 g delivered); 25% glucose was infused (3.0 g delivered) for the two remaining infusions. For each concentration, gastric contents were withdrawn either immediately or 30 min after infusion offset. The tests were delivered in counterbalanced order across rats. Results were analyzed via a three-way [group (GVX/intact) x concentration x sample latency (0 and 30 min)] ANOVA, with amount of glucose emptied as the dependent measure. The same ANOVA model was used with infusate volume emptied as the dependent measure.

RESULTS

Experiment 1

Three out of ten prospective GVX subjects were rejected from the study on the basis of histological analysis. In each of the rejected cases, cells containing fluorescent label, indicating retrograde transport of fluorogold (see METHODS), were found on one side in the central subregion of the DMN.

GVX and intact rats consistently consumed all or almost all of the daily 40-ml diet allotment. Body weights of GVX (mean 282 g) and intact rats (mean 294 g) did not differ significantly (t = 0.749, nonsignificant) at the end of the experiment, 16–21 days after surgery.

Figure 1 shows glucose emptied (in g) for control (solid line) and GVX rats (dashed line) where gastric samples were taken at different points (0, 18, and 36 min) after the offset of 18-min intragastric infusions. It is clear from a comparison of the values at time zero postinfusion that considerably more glucose had emptied over the course of the infusion in GVX than in intact rats (57.4 and 36.4% of the solute delivered had emptied during fill in GVX and intact rats, respectively). Emptying rate slowed dramatically after infusion offset for both groups. The increment in glucose emptied from 0–36 min after fill was considerably less than the amount emptied during the 18-min fill period. Importantly, the rate of emptying in the postfill period was similar for both groups, as is apparent from the nearly parallel emptying curves in Fig. 1. These points are substantiated by the two-way ANOVA on this data set that revealed a main effect of group [GVX vs. intact, F(1,10) = 11.27, P < 0.01] and sample latency [F(2,20) = 35.12, P < 0.001], but no significant two-factor interaction [F(2,20) = 1.34, nonsignificant].

The two pairs of bars on the left of Fig. 2 show the amount of glucose emptied for control (filled bars) and GVX (open bars) rats where gastric samples were taken either immediately or 9 min after offset of 9-min
infusions. The two-way ANOVA for this data set reveals parallels with the results described above for the 18-min infusion conditions. 1) Amount emptied was higher in GVX than in control rats, as indicated by a significant main effect of group \( F(1,10) = 16.32, P < 0.01 \). 2) The small overall increment in glucose emptied over the 9 min after infusion offset just failed to reach significance at the 0.05 level [main effect of sample latency, \( F(1,10) = 4.42, P = 0.062 \)]. The interaction term for group and sample latency factors was not significant \( F(1,10) = 2.88, P = 0.12 \), indicating that the GVX effect was fully expressed by the end of the infusion and that the emptying rates thereafter did not significantly differ as a function of GVX.

An additional point can be raised via selected comparisons between the data sets for the 9- and 18-min infusions. It appears for both GVX and control rats that the rate of gastric emptying remains roughly stable throughout the course of an 18-min infusion, insofar as the amounts emptied at the halfway point (sample taken directly after 9-min infusions) is about one-half that measured for the sample taken at the end of the extended infusion (compare 9:9 and 18:18 in Fig. 2). In addition, considerably more glucose had emptied for both groups for the samples withdrawn at the end of an 18-min infusion than when withdrawn 9 min after a 9-min infusion (compare 9:18 and 18:18 in Fig. 2). This finding indicates that for both groups the transition from a high to a low rate of emptying was at the offset of the 18-min infusion (compare 9:18 and 18:18 in Fig. 2). In absolute terms, the increased amount emptied through the course of an 18-min infusion, insofar as the rate of gastric emptying remains roughly stable throughout the course of an 18-min infusion, both groups for the samples withdrawn at the end of an 18-min infusion than when withdrawn 9 min after a 9-min infusion (compare 9:18 and 18:18 in Fig. 2). In absolute terms, the increased amount emptied in GVX than in control rats \( [F(1,11) = 46.75, P < 0.001] \). Emptying also varied significantly with stimulus concentration \( [F(1,11) = 51.10, P < 0.001] \). It is apparent from inspection of the values for samples taken directly after infusion offset that, for each group, the amount of glucose emptied during fill approximately doubled with the doubling of stimulus concentration. In absolute terms, the increased amount emptied for GVX rats was greater than the increase in controls, resulting in a significant group \( \times \) concentration interaction \( [F(1,11) = 8.43, P < 0.02] \). These effects were fully expressed in the first postinfusion sample point. Thus, although there was a significant increment in amount emptied from 0 to 30 min postinfusion \( [F(1,11) = 25.15, P < 0.001] \), the magnitude of that increment did not vary either as a function of concentration or of group. This conclusion is evident from the generally parallel appearance of the four lines in Fig. 3 and is reinforced by the lack of any significant interaction involving the sample time factor [sample time \( \times \) group, \( F(1,11) = 1.90 \), nonsignificant; sample time \( \times \) concentration, \( F(1,11) = 3.55 \), nonsignificant; 3-factor interaction, \( F(1,11) = 0.122 \), nonsignificant].

Figure 4 shows the volume of infusate emptied for the samples withdrawn at the end of the 12-min infusions for GVX and control rats. As for the ANOVA on solute emptied, a significant overall effect of GVX.

Experiment 2

None of the prospective GVX subjects were rejected from this experiment on the basis of the postmortem analysis.

GVX and intact rats consumed all or almost all of the daily 40-ml diet allotment. Mean body weights of GVX and intact rats differed by \(<1 \text{ g} \) (overall mean 266 g) at the end of the experiment. The experiment was completed 18–20 days after surgery, with one exception. One intact rat required retesting of several conditions because of leakage between the infusion tube insert and the inner threading of the gastric fistula and completed the experiment on its 23rd postsurgical day.

Figure 3 shows the amount of glucose emptied in GVX and control rats as functions of sample time (0 and 30 min) after the termination of 12-min intragastric infusions and of infusate concentration (12.5 and 25%). For each concentration, considerably more glucose was emptied in GVX than in control rats \( [F(1,11) = 46.75, P < 0.001] \). Emptying also varied significantly with stimulus concentration \( [F(1,11) = 51.10, P < 0.001] \). It is apparent from inspection of the values for samples taken directly after infusion offset that, for each group, the amount of glucose emptied during fill approximately doubled with the doubling of stimulus concentration. In absolute terms, the increased amount emptied for GVX rats was greater than the increase in controls, resulting in a significant group \( \times \) concentration interaction \( [F(1,11) = 8.43, P < 0.02] \). These effects were fully expressed in the first postinfusion sample point. Thus, although there was a significant increment in amount emptied from 0 to 30 min postinfusion \( [F(1,11) = 25.15, P < 0.001] \), the magnitude of that increment did not vary either as a function of concentration or of group. This conclusion is evident from the generally parallel appearance of the four lines in Fig. 3 and is reinforced by the lack of any significant interaction involving the sample time factor [sample time \( \times \) group, \( F(1,11) = 1.90 \), nonsignificant; sample time \( \times \) concentration, \( F(1,11) = 3.55 \), nonsignificant; 3-factor interaction, \( F(1,11) = 0.122 \), nonsignificant].

Figure 4 shows the volume of infusate emptied for the samples withdrawn at the end of the 12-min infusions for GVX and control rats. As for the ANOVA on solute emptied, a significant overall effect of GVX.
was obtained \( [F(1,11) = 31.86, P < 0.001] \). Glucose concentration, however, did not affect volume emptied \( [F(1,11) = 1.35, \text{nonsignificant}] \), and there was no significant two-factor (concentration \( \times \) group) interaction \( [F(1,11) = 0.13, \text{nonsignificant}] \).

**DISCUSSION**

GVX greatly accelerated the rate at which glucose emptied from the rat’s stomach. The GVX effect under the conditions tested, however, was entirely restricted to the period of gastric fill. The dissociation of the GVX effect with respect to the fill and postfill periods offers suggestions about which emptying control processes were and were not disrupted by gastric vagotomy and supports the hypothesis (see Ref. 17) that there are two distinct phases of normal emptying control with contrasting physiological underpinnings.

The lack of a GVX effect on glucose emptying in the postfill period suggests that feedback regulatory controls were equally evident and equally effective in control and GVX rats (19, 20). Thus solute emptying rate in the postfill period for both groups was stable over time (linear emptying function) and not affected by a doubling (12.5 to 25%) of infusate concentration. Such feedback control entails a sensory signal carrying information related to the amount of glucose emptied. It is perhaps not surprising that a gastric vagotomy would not interfere with such feedback arising from postgastric sources. The indication that gastric vagal efferents do not appear necessary for a normal-like emptying of glucose after fill, however, is challenging. Feedback influences on fluid emptying are mediated by adjustments in gastric tone, intragastric pressure (29), pyloric action, and/or duodenal pressure, and it is generally acknowledged that gastric vagal efferents are potent modulators of each of these gastromotor variables (2, 3).

It is also clear, however, that there are other sources of gastromotor control, including splanchnic efferents, a projection to the antrum and pylorus from the hepatic branch of the vagus nerve, circulating hormones, and intrinsic neurons (6, 13, 14). It appears likely that one or more of these sources represent the gastromotor limb of the feedback control mechanism in GVX rats. The normal-like postfill emptying profile in GVX rats is consistent with the suggestion that gastric vagal efferents play no necessary role in feedback control of glucose emptying under physiological conditions in the intact rat. It is also possible, however, that the gastric vagal efferents are an important mediator of feedback influences on gastric emptying under normal conditions, with other gastromotor systems compensating for their loss after GVX. The plausibility of adaptive changes after vagotomy is supported by the work of Andrews et al. (2). They showed, in the ferret, that an effect of splanchnicectomy, a marginal increase in the intragastric pressure response to fluid inflation, was accentuated if the cervical vagus had been previously sectioned.

The dramatic increase in the rate of solute emptying during stomach fill in GVX rats indicates the disruption of an emptying-inhibitory mechanism that operates exclusively during this period. It is important to note, however, that despite the prominent group difference, several features of normal control of emptying during fill were entirely unaffected by GVX. In both control and GVX rats, the rate of glucose solute emptying was considerably higher during fill than after fill. Results of experiment 1 showed for both groups that the abrupt transition from a high to low emptying rate coincided specifically with the offset of the intragastric infusion, regardless of its duration (9 or 18 min) and of how much glucose had cumulatively emptied. The idea that initially rapid emptying reflects a “rush” that lasts until feedback control is achieved is thereby discounted (see Ref. 17 for discussion). It is also clear that the type of regulatory control operating in the postfill period did not apply to emptying during fill in either intact or GVX rats. Thus, for both groups, glucose solute emptying rate was not held constant when glucose concentration was increased. In fact, solute emptied during fill in both GVX and control rats almost doubled when glucose concentration was doubled from 12.5 to 25% (Fig. 3). For both groups, it was the volume, rather than solute, emptied during fill that remained stable when stimulus concentration was increased (compare open and hatched bars in Fig. 4). This observation is consistent with the suggestion (see Ref. 17) that the effect of concentration manipulation on solute emptying is a passive outcome of the action of mechanism(s) that control the volume that empties from the stomach during fill. In this light, a simple characterization of the GVX effect on emptying during fill can be offered. GVX apparently disrupts the mechanism that restrains emptying on a volume basis during stomach fill. After GVX, volume emptied was increased substantially and to approximately the same extent for the two glucose concentrations infused.

One mechanism that may contribute to restraining gastric emptying during fill is the “receptive (or adaptive) relaxation” response to increases in stomach volume (8). The response is a decrease in gastric tone that opposes an increase in gastric pressure that would otherwise arise from continued filling of the stomach. Without an effective receptive relaxation response, one would expect (29) the increased intragastric pressure to precipitate a greater rate of gastric emptying of fluids during fill. Although nonvagal factors (e.g., enteric (25)) may participate, several studies indicate that receptive relaxation entails a gastro-gastric vago-vagal reflex arising from stimulation of gastric mechanoreceptors (1, 7, 9, 11). These findings are consistent with the suggestion that the increase in emptying during fill in GVX rats reflects disruption of the receptive relaxation response. It is also possible that a relaxation response to distension of the duodenum and intestine (10) participates in the restraint of emptying during fill under normal conditions. If this is the case, then disruption of the efferent limb of this accommodative reflex by GVX may contribute to the accelerated glucose emptying during fill. Additional work is required to determine which relaxation response entailing gastric vagal efferent mediation, or which other mechanism, accounts in
greatest part for the increased volume emptied during fill in GVX rats.

Perspectives

It is clear from the preceding discussion that further work is required to parse the vagal (gastric and postgast- rich, afferent and efferent) and nonvagal contributions to emptying control. From our perspective, such work should proceed with attention to the distinction between controls of gastric emptying during vs. after fill. The indication that separable physiological processes underlie emptying during these phases can help identify specific functions that are and are not influenced by treatments of interest. Protocols involving the delivery of a bolus to the stomach or intestine with the first (or only) gastric sample taken some time after stimulus delivery are not well suited for distinguishing the controls of emptying during and after fill. Insofar as most available data concerning neural and hormonal influences on gastric emptying were collected in this manner, replications with more discriminating designs appear to be in order.

The lack of a GVX effect on glucose emptying in the postfill period does not permit the inference that the emptying of nutritive fluids other than glucose would be similarly unaffected by GVX. In recent years, evidence has mounted suggesting that separable afferent pathways underlie feedback control of gastric emptying for different nutrients. For example, the extent to which gastromotor responses to duodenal infusion are reduced after capsaicin deafferentation of vagal or splanchnic nerves varies as a function of the type of nutrient infused (12, 23, 24). Whether effenter pathways are differentially involved in feedback control for different nutrients is an issue yet to be examined systematically. This possibility would be raised if, in contrast to the present results for glucose, GVX accelerated postfill emptying of proteins, fats, or mixed fluid meals. Interpretation of such experiments should be tempered by a recognition that a GVX effect might reflect not only a disruption of efferent mediation of feedback control, but also a disruption of the sensory signal. It has been shown that cholecystokinin (CCK) is released on duodenal delivery of fats, protein, and certain carbohydrates (glucose not among them), and it is suggested that this release represents a hormonal link in the feedback control of emptying for these stimuli (12, 24). Caution is indicated for the interpretation of effects of GVX on emptying of such stimuli, insofar as this hormonal link may entail stimulation of CCK receptors on gastric vagal afferents (9, 27, 28). Selective denervations of gastric vagal afferents and efferents (22, 30) would offer a more discriminating approach to the nutrient specificity of sensory and gastromotor elements of feedback inhibitory control.

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