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Am J Physiol Gastrointest Liver Physiol, October 1, 2007; 293 (4): G692-G698.
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Effects of intraduodenal glucose infusion on gastric myoelectrical activity and antropyloroduodenal motility

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Verhagen, M. A. M. T., M. Samsom, and A. J. P. M. Smout. Effects of intraduodenal glucose infusion on gastric myoelectrical activity and antropyloroduodenal motility. *Am. J. Physiol.* 274 (*Gastrointest. Liver Physiol.* 37): G1038–G1044, 1998.—Intraduodenal nutrient infusions cause an inhibition of antral motility and an increase in pyloric motility. The involvement of gastric myoelectrical activity in this intestinogastric feedback was studied. Electrogastrography and antropyloroduodenal manometry were performed in 10 healthy volunteers. The effects of 20-min infusions of 25% glucose (4 kcal/min) and saline were compared. Intraduodenal glucose infusions caused a decrease in the power of the dominant frequency in the electrogastrogram ($P = 0.028$), but the frequency itself remained unchanged. The total number of dysrhythmias increased ($P = 0.035$). An inhibition of antral motor activity ($P = 0.001$), an increase in the number of isolated pyloric pressure waves ($P = 0.027$), and an increase in basal pyloric tone ($P = 0.001$) were simultaneously recorded. The change in power during glucose infusion correlated positively with the change in the antral motility index ($r_s = 0.50$, $P = 0.001$). It is concluded that inhibition of gastric myoelectrical activity is one of the mechanisms underlying an inhibition of motor activity in the gastric antrum.

electrogastrography; antropyloroduodenal manometry; duodenogastric reflex

GASTRIC EMPTYING is determined by an integrated motor activity of the proximal stomach, antrum, pylorus, and proximal duodenum (6, 8, 11, 26, 31, 35, 50). The proximal stomach relaxes after food ingestion, allowing the accommodation of food, and an increase in tone of the proximal stomach enhances the gastric emptying of fluids (35). Lumen-occlusive contractions of the antrum propagate gastric contents into the duodenum and, when the pylorus is closed, help to mix and grind the food in the stomach (8, 31). Pyloric contractions prevent food from entering the duodenum (31, 50).

Feedback mechanisms from the duodenum to the stomach play an important role in the regulation of gastric emptying. Infusion of different types of nutrients (glucose, lipid, amino acids) directly into the duodenum causes relaxation of the proximal stomach, inhibition of the contractile activity of the antrum, and an increase in the tonic and phasic activity of the pylorus (14, 16, 18–20, 24–27, 29). These effects result in a delay of gastric emptying (19, 26, 50). The exact mechanisms behind these intestinogastric motor responses are still poorly understood.

Gastric myoelectrical activity is one of the mechanisms regulating the contractile activity of the stomach (48). The myoelectrical activity of the stomach is characterized by rhythmic activity of ~3 cycles per minute (cpm) (30) and can be recorded with the use of cutaneous electrodes, a technique called electrogastrography (EGG) (47). We hypothesized that intraduodenal glucose infusion influences gastric myoelectrical activity, which may alter gastric motor function.

The aim of this study was therefore to investigate the involvement of gastric myoelectrical activity in intestinogastric feedback mechanisms and its relation to changes in gastric and pyloric motor activity during intraduodenal glucose infusion.

MATERIALS AND METHODS

Subjects. Ten healthy volunteers (3 female, 7 male; median age 23 yr, range 21–32) were enrolled. Subjects were excluded when medical history or physical examination revealed symptoms of systemic or gastrointestinal disease or when medication was used. Smoking was prohibited on the study day. Written informed consent was given, and the protocol was approved by the ethics committee of the University Hospital Utrecht.

Experimental protocol. After an overnight fast, a water-perfused antroduodenal manometric assembly was introduced transnasally and positioned across the pylorus by monitoring the transmucosal potential difference (TMPD). The subjects were positioned in a bed with the head of the bed elevated 45 degrees. When the manometric catheter was positioned correctly, the EGG recordings were started. After a recording period of at least 30 min, two 20-min periods followed, during which 25% glucose and saline were given intraduodenally in a random order at a rate of 4 ml/min (4 vs. 0 kcal/min). Each infusion started during a well-defined phase II and was followed by a washout period of at least 45 min.

Electrogastrography. The EGG recording technique used in this study has been described previously (7, 33). In brief, four differential recordings of gastric myoelectrical activity were made from five disposable pregelled Ag-AgCl surface electrodes placed at standard positions on the upper abdomen, with a reference electrode on the right ankle (33). The signals were band-pass filtered (0.6–30 cpm), converted from analog to digital (sample frequency 4 Hz), and stored on-line on the hard disk of a computer for later analysis.

The EGG signals were subjected to running spectrum analysis. Subsequent 256-s signal stretches that overlapped by 196 s were subjected to a fast Fourier transform, using a Hamming window. Zero padding was used to decrease the frequency distinction level from 0.234 to 0.059 cpm: after the Hamming window was applied to the 256-s signal stretch, a 768-s stretch of zeros was added. The spectral analysis was performed on the 1,024-s stretch obtained.

Of the resulting power spectra (0–120 cpm), the frequencies between 0 and 15 cpm were visualized. The mean of all power spectra for each channel was calculated, and the EGG signal with the highest power in the 3-cpm (2.6–3.7 cpm) band was selected for further analysis. The mean frequency of the normal 3 cpm (2.6–3.7) component, its standard deviation, and its power content (μV^2) were calculated over 10-min intervals. Power ratios were calculated with respect to the fasting period preceding the infusions or the meal. The frequency instability coefficient was defined as the standard

deviation divided by the mean frequency of the dominant peak. Higher harmonics were defined as sharp peaks in the spectra, which occur at exact multiples of the fundamental frequency and have a power of at least 5% of this fundamental component (33). Tachygastrias were defined as sharp-peaked components in the frequency spectrum occurring at a frequency >3.7 and <11 cpm, not being higher harmonics (10, 33). For a definite diagnosis of tachygastria it was necessary for the abnormal frequency to last more than 2 min and for a normal gastric signal to be absent in all four EGG signals. When an abnormal frequency lasted less than 2 min or when a normal 3-cpm rhythm was also visible, tachygastria was considered probable (33). Bradygastrias were defined as sharp peaks in the spectrum at frequencies <2.6 cpm that were not caused by movement artifacts.

Manometry. Antropyloroduodenal manometry was performed with the use of an 11-lumen silicone water-perfused assembly with a 4.5-cm pyloric sleeve (OD 4.4 mm, ID of manometric lumina 0.75 mm; Dentsleeve, Adelaide, Australia). The sleeve was positioned across the pylorus. Four side holes (*A4, S1, S2, D1*) were spaced at 1.5-cm intervals along the sleeve length. Three additional antral side holes (*A1–A3*) were positioned at 1.5-cm intervals proximal to the sleeve, and another two side holes in the duodenum were spaced 3 (*D2*) and 13 cm (*D3*) from the distal end of the sleeve. To monitor the position of the catheter, the two side holes at each end of the sleeve (*A4* and *D1*) were perfused at 0.3 ml/min with degassed saline, and the transmucosal difference between antrum and duodenum was measured (28). All other recording side holes were perfused with degassed water at a rate of 0.3 ml/min. An infusion port was positioned 15 cm from the distal end of the sleeve. Three tungsten weights were attached to the distal end of the catheter to facilitate positioning.

Pressure signals were measured by external transducers (DPT-200; Utah Medical), sampled at a frequency of 4 Hz, and stored in a data logger (Medical Measurement Systems, Enschede, The Netherlands). TMPD signals were sampled at 1 Hz and stored in the same data logger. A personal computer served as an on-line monitoring and retrieval system.

Pressure signals were analyzed quantitatively, using commercially available software (Medical Measurement Systems, Enschede, The Netherlands). The number of pressure waves with an amplitude ≥1.4 kPa (10 mmHg) and their mean amplitude were calculated after elimination of artifacts caused by abdominal pressure peaks, respiration, and drift of the transducers (42). The motility index was defined as ln[(number of contractions × sum amplitudes) + 1].

Phase II activity was defined as two or more pressure waves in 10 min but fewer than 10–12 pressure waves per minute (the maximum frequency of the duodenum). Pyloric

tone was defined as the difference between the basal pressure recorded by the sleeve and that in the distal antrum (29). Isolated pyloric pressure waves (IPPWs) were defined as pressure waves with an amplitude ≥1.4 kPa recorded by the sleeve in the absence of an associated wave in one of the TMPD side holes within 5 s, with a recorded pressure wave in no more than one side hole between the TMPD side holes (29).

Sensations. Sensations (nausea, abdominal pain, bloating, satiety, and hunger) were recorded on a 100-mm visual analog scale at regular intervals during the intraduodenal infusions and after the meal.

Analysis. Electrogastrographic and manometric data were calculated in 10-min and 20-min intervals, starting 20 min before the infusion until 20 min after each infusion. The 20-min intervals before each infusion were considered as baseline periods for the subsequent periods. Manometric data were analyzed only when the TMPD signals indicated a correct position of the catheter.

Nonparametric tests were used in the statistical analysis, using the Friedman ANOVA and Wilcoxon's signed-rank test for related samples (SPSS for Windows 6.1). ANOVA with repeated measures was performed after logarithmic transformation of the data. Spearman rank correlations were calculated. Significance was accepted with a P value ≤0.05. Unless stated otherwise, values are given as medians with interquartile range.

RESULTS

Sensations. The study was well tolerated by all subjects. During the infusion of both glucose and saline, the median scores for the individual sensations of nausea, abdominal pain, bloating, and satiety were all 0 mm (maximum score 7 mm). The median score for hunger was 13 mm (4–24 mm) during glucose infusion and 15 mm (3–27 mm) during saline infusion. No significant differences were found between the sensations reported during the infusion of glucose and the infusion of saline (not significant, for all comparisons).

EGG parameters. In the analysis of the individual spectra, a clearly defined peak could be identified in 92% of the spectra (96% of the fasting spectra; 90% of the spectra during infusion; 90% of the first 20 spectra after infusion).

Figure 1 shows a typical example of an EGG recording during glucose infusion and during saline infusion. Glucose infusion induced a decrease in the power of the dominant EGG frequency which lasted until the first 10 min after the infusion period; this decrease was not
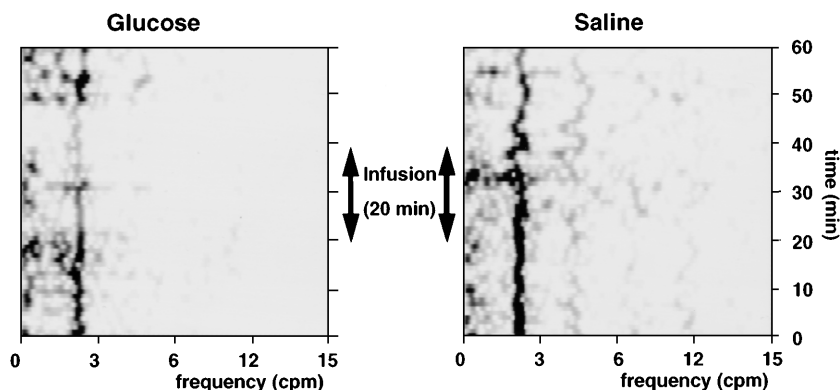

Fig. 1. Running spectrum analysis of electrogastrography (EGG) signals recorded during infusion of glucose and infusion of saline, showing a decreased power of the dominant EGG frequency with glucose. cpm, Cycles per minute.

Fig. 2. Changes in EGG power in 10-min intervals; 0–10 and 10–20 indicate period during infusion; 20–30 and 30–40 indicate periods after infusion. * $P < 0.05$ vs. saline; + $P < 0.05$ vs. baseline.
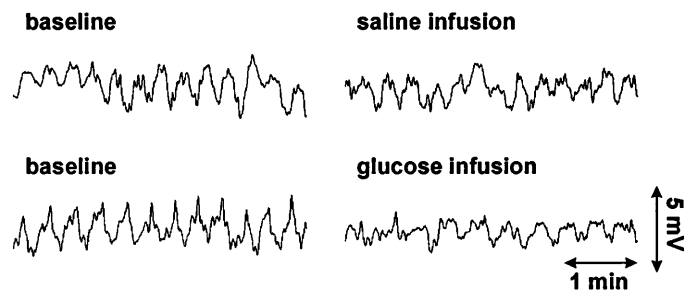

Fig. 3. EGG signals (4-min stretches) recorded before and during intraduodenal infusion of saline and glucose. Glucose infusion caused a decrease in signal amplitude and induced bradygastrias.

observed during saline infusion ($P = 0.028$; Fig. 2). Results of the analysis of the 20-min intervals during and after intraduodenal infusions are shown in Table 1. No significant changes were found in the mean dominant frequency either during or after the infusion period of glucose and saline. A higher frequency instability coefficient was found after glucose infusion compared with saline ($P = 0.016$).

A significant increase in the number of bradygastrias was seen during the 20-min period after infusion compared with the baseline period before infusion ($P = 0.043$) but not compared with the saline infusion period ($P = 0.074$; Fig. 3). Saline caused no significant increase in bradygastrias compared with the baseline period. The percentages of tachygastrias and probable tachygastrias during and after glucose infusion were low and comparable to saline infusion both during and after the intraduodenal infusion period. An increase in the total number of dysrhythmias with intraduodenal glucose infusion compared with saline was found when the periods during and after infusion were taken together ($P = 0.035$). The number of dysrhythmias was significantly increased in the period after glucose infu-

sion ($P = 0.043$ vs. saline, $P = 0.027$ vs. baseline period).

Manometry. The TMPD measurement indicated a correct position of the catheter >99% of the time. A typical example of the effects of intraduodenal glucose infusion is shown in Fig. 4. Intraduodenal glucose infusion induced a decrease in the number of antral pressure waves ($P = 0.007$) and in the antral motility index ($P = 0.001$) compared with saline (Fig. 5). Both the number of IPPWs ($P = 0.027$) and the basal pyloric tone increased ($P = 0.001$) during glucose infusion and returned to normal afterwards (Fig. 5). Motility parameters over the 20-min periods are given in Table 2. A significant decrease in the number of contractions both during and after the infusion was also found in the proximal duodenal channels (*D1*, $P = 0.016$; *D2*, $P = 0.006$). In the third duodenal channel glucose initiated a short increase in activity, resembling phase III-like activity, resulting in a higher motility index during the first 10 min of glucose infusion ($P = 0.037$). But later an inhibition of motility in this channel was found ($P = 0.013$; Table 2). An increase in duodenal motility was found during saline infusion compared with the preceding baseline period.

The change in power during glucose infusion correlated positively with the change in the antral motility index ($r_s = 0.50$, $P = 0.001$).

Table 1. *EGG data*

	Glucose		Saline	
	During infusion	After infusion	During infusion	After infusion
Change in power, mV^{-8}	−1.88*†	−1.42*†	−0.37	−0.64
	(−9.9 to −1.02)	(−5.47 to −0.55)	(−1.82–0.00)	(−2.84–0.05)
Frequency, cpm	2.80	2.92	2.80	2.84
	(2.68–2.90)	(2.77–3.09)	(2.65–2.99)	(2.64–2.97)
Instability coefficient (10^{-2})	8.01*	8.17	5.49	7.02
	(5.99–9.53)	(5.95–11.1)	(4.48–6.09)	(6.06–8.75)
%Harmonics	9	4	11	11
	(0–29)	(0–24)	(0–33)	(0–38)
%Bradygastrias	0	3	0	0
	(0–17)	(0–50)	(0–2)	(0–12)
Total %tachygastrias and probable tachygastrias	1.68	2.2	1.7	0.6
%All dysrhythmias	3†	13*†	0	0
	(0–27)	(0–53)	(0–8)	(0–12)

Because the number of tachygastrias and probable tachygastrias was less than 1% in most individuals, only the total percentage of all spectra in all individuals is given. EGG, electrogastrography; cpm, cycles per minute. * $P < 0.05$ vs. saline. † $P < 0.05$ vs. baseline.
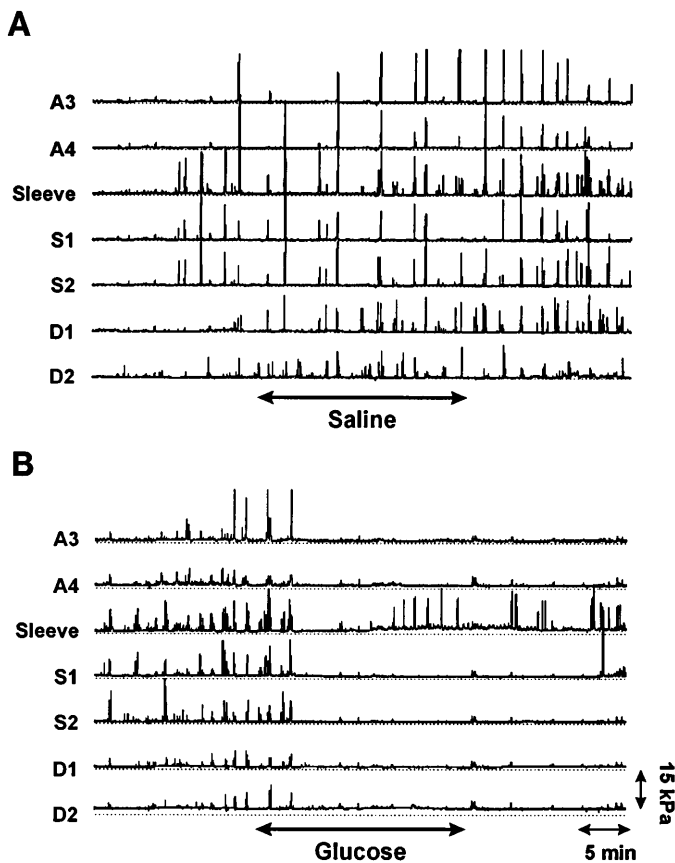
A

B

Fig. 4. Example of manometric recordings during infusion of saline and infusion of glucose. Saline infusion did not change antropyloroduodenal motility (*A*). During glucose infusion (*B*) basal pyloric tone and number of isolated pyloric pressure waves increased and antral motility was inhibited. The transmucosal potential difference measurement indicated a correct position of the catheter during the whole measurement period. *A3* and *A4*, antral channels; *S1* and *S2*, channels along the sleeve; *D1* and *D2*, duodenal channels.

DISCUSSION

In this study we have shown that intraduodenal glucose infusion decreases the power of gastric myoelectrical activity and that the frequency of the EGG signal becomes less stable during intraduodenal glucose infusion, as evidenced by an increase in the total number of dysrhythmias and a higher frequency instability coefficient. We have confirmed that, manometrically, intraduodenal glucose infusion inhibits the contractile motor activity of the gastric antrum and proximal duodenum and simultaneously increases both pyloric tone and phasic pyloric activity (27, 29). The change in power of the EGG was positively correlated with the change in antral motility.

Although the amplitude of the cutaneous EGG signal has been shown to depend on several factors, such as electrical resistance of the skin and surface area of the electrodes (38, 39), two main factors are held responsible for changes in power during EGG recordings (9, 40, 48). First, the power of the EGG has been shown to be related to the extent of motor activity and electrical response activity in the stomach (48). Second, changes in power can also be caused by changing the distance

between the recording electrodes and the gastric wall (40). In our study the decrease in power of the EGG is not likely to be caused by a change in the position of the stomach, because the intraduodenal infusions probably did not affect the filling of the stomach. Moreover, intraduodenal nutrient infusion causes a relaxation of the fundus and a closure of the pylorus. These changes could lead to a displacement of the stomach toward the abdominal wall, which, however, would have resulted
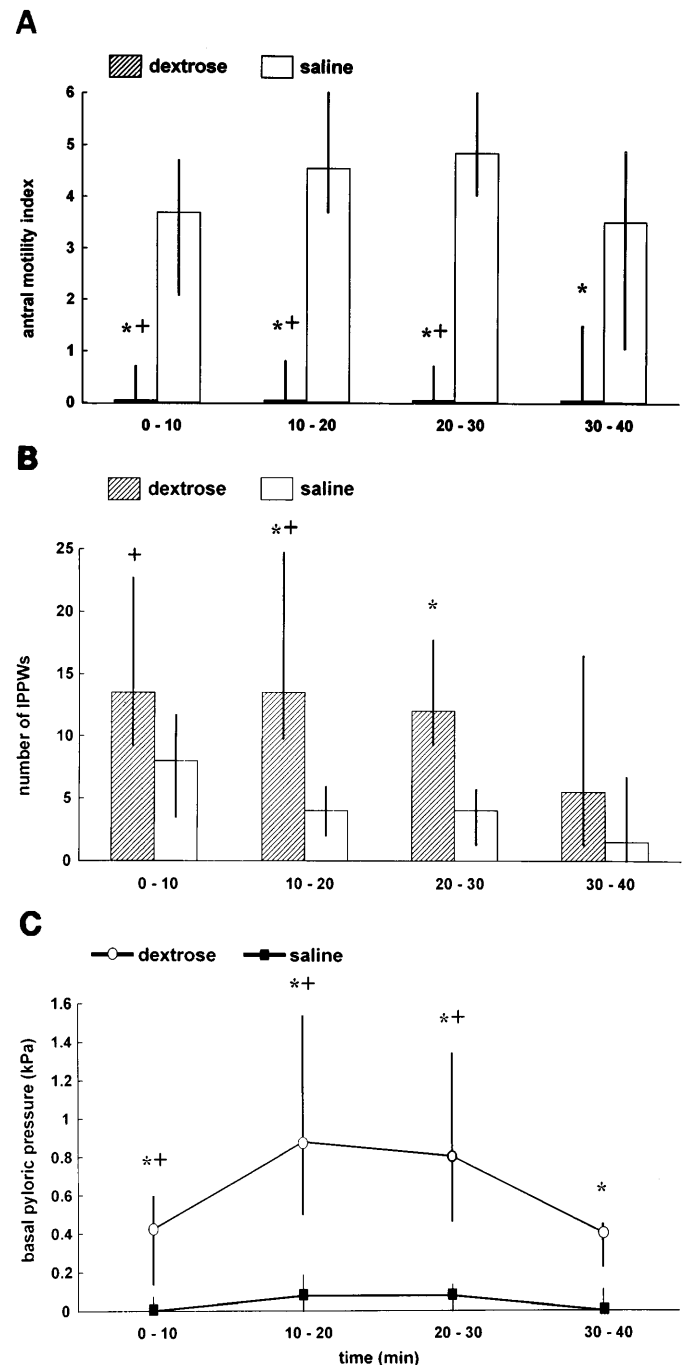
A

B

C

Fig. 5. Antral and pyloric motility in 10-min intervals; 0–10 and 10–20 indicate period during infusion; 20–30 and 30–40 indicate periods after infusion. *A*: antral motility index. *B*: number of isolated pyloric pressure waves. *C*: basal pyloric pressure. * $P < 0.05$ vs. saline; + $P < 0.05$ vs. baseline.

Table 2. *Manometry data*

	Glucose		Saline	
	During infusion	After infusion	During infusion	After infusion
Antral MI	0.00* (0.00–0.94)	0.84* (0.00–3.55)	6.46 (4.79–6.97)	5.99 (5.49–7.44)
Basal pyloric tone, kPa	0.64*† (0.44–1.34)	0.61*† (0.36–0.86)	0.04 (0–0.11)	0 (0–0.11)
IPPWs	34*† (17–40)	18* (16–28)	13 (5–23)	7 (3–10)
Duodenal MI *D1*	1.78* (0.24–5.56)	2.46*† (0–3.99)	6.48 (5.99–8.21)	6.64 (3.56–9.10)
Duodenal MI *D2*	5.40* (4.12–7.81)	5.24* (3.51–7.38)	8.93† (8.21–9.46)	7.21 (6.44–9.95)
Duodenal MI *D3*	9.35† (8.54–9.99)	3.40* (2.16–5.03)	7.93† (7.04–8.81)	7.71† (6.43–9.05)

Values for isolated pyloric pressure waves (IPPWs) are given as number per 20 min. MI, motility index. *D1, D2,* and *D3* are side holes; see text for further description. * $P < 0.05$ vs. saline; † $P < 0.05$ vs. baseline.

in an increase of the EGG power rather than a decrease. The decrease in power was also found to be correlated with a decrease in antral activity. Thus the decrease in antral activity is reflected by a decrease in the power of the EGG. Observations in dogs, in which intraduodenal lipid infusions caused a decrease in electrical response activity, support these findings (15).

Intraduodenal glucose also influenced the frequency of the EGG. We found an increase in bradygastrias and a less stable dominant frequency. An increase of bradygastrias during intraduodenal lipid infusions has also been reported in humans (24), whereas in dogs the frequency of the electrical control activity increased during intraduodenal lipid infusions (16). These findings represent an effect on the gastric pacemaker.

During intraduodenal glucose infusion pyloric contractility was stimulated and antral motility was inhibited. Since these are opposite effects it is very unlikely that this is caused by a direct effect on the smooth muscle cells. In humans the effects of intraduodenal nutrient infusion are sensitive to atropine (20, 29). Thus extrinsic and intrinsic neural mechanisms are involved in intestinogastric feedback mechanisms, a finding supported by experiments in animals (1, 13, 51).

Humoral factors are also involved, as the effect of intraduodenal glucose infusion lasted until ~10 min after infusion. We did not measure blood glucose, but other studies have shown that intraduodenal glucose infusion causes a rise in blood glucose levels (14, 36). Hyperglycemia has been shown to delay gastric emptying (17, 22, 41, 46), inhibit antral motility (2, 3, 21, 41), induce tachygastrias (23, 33), increase the number of IPPWs (21), and disturb intestinal motility (3, 17, 21). Gastric emptying and antral motility are also affected by changes in the glucose levels within the physiological range (<10 mmol/l) (2, 34). These effects of hyperglycemia are likely to be mediated through a neural pathway (12). The effects of hyperglycemia are very

similar to some of our findings, but it cannot be concluded that the effects induced by intraduodenal glucose are solely caused by hyperglycemia. Intraduodenal infusion of lipid causes similar effects on the motor activity of the antrum, pylorus, and duodenum (27, 28). Moreover, the main abnormalities in the EGG during hyperglycemia are tachygastrias (23, 33), and these abnormalities were only found during marked hyperglycemia (>10 mmol/l) (23). In this study the most predominant effects on the EGG were a decrease in power and an increase in the number of bradygastrias. Hebbard et al. (24) reported an increase in the number of bradygastrias during intraduodenal lipid infusion. The same study showed an increase in tachygastrias only when lipid was infused during hyperglycemia (24). Lavin et al. (36) showed that blood glucose levels are not responsible for the change in appetite during intraduodenal glucose infusion in healthy volunteers. Thus, although acute hyperglycemia might have influenced our results, other humoral mechanisms are likely to be involved.

During intraduodenal glucose infusion a number of hormones are released, such as insulin and glucagon-like peptide-1 (GLP-1) (36, 43, 49). These hormones delay gastric emptying (4, 17, 43, 52) and inhibit antral motility (4, 17, 44, 45). Thus intestinal hormones are also likely to play a role in the intestinogastric feedback mechanisms. The exact interaction between neural pathways, glucose levels, and intestinal hormones has not yet been clarified.

The 25% solution of glucose was chosen because this concentration has been shown to have clear effects on gastric and pyloric motility (29). The infusion rate of 4 kcal/min is above the mean physiological rate of gastric emptying, which is considered to be 2.1–2.5 kcal/min, as a mean value over a longer period (5, 32). The same studies, however, also showed that during the initial phase of gastric emptying higher emptying rates (up to 4 kcal/min) occur (5, 32). Therefore this infusion rate can be considered to be physiological during the initial phase of gastric emptying, when feedback mechanisms are not yet activated.

There was an approximately fourfold difference in osmolarity between saline and glucose. Thus the effects of intraduodenal glucose might be due to stimulation of osmoreceptors in the duodenum instead of glucoreceptors. However, several studies have shown that the osmolarity of a solution administered intraduodenally is not a major contributor compared with the effect of glucose (5, 29, 37).

We also recorded a decrease in motor activity of the duodenum, suggesting that not only is the stomach involved in the inhibitory feedback, but the duodenum is involved as well. The short increase in motility that was recorded after the infusion of glucose has been described previously (18, 29). However, only limited information on duodenal motility could be obtained from this study, since two of the channels were positioned in the duodenal bulb and the third was located 2 cm proximal to the infusion opening.

In conclusion, we have shown that gastric myoelectrical activity is inhibited by intraduodenal nutrient

infusion and that this is one of the mechanisms underlying an inhibition of contractile activity of the gastric antrum.

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