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The use of gastric electrical signals for algorithm for automatic eating detection in dogs

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Abstract *Food ingestion increases fundic impedance (FI) and reduces antral slow wave rate (SWR). Our aim was to determine if such changes can be integrated into an algorithm for automatic eating detection (AED). When incorporated in implantable medical devices, AED can time treatment to food intake without need for patient input. Four dogs were implanted with fundic and antral electrodes, connected to an implantable recording device. Changes in FI and SWR induced by fixed meals of different weights were determined, and were used to build an AED algorithm. Its performance was then tested on the same animals given an ad libitum access to food. The effects of gastric balloon distension and nitroglycerin on SWR and FI were also tested. Fixed meals reduced SWR in a weight-dependant manner,* $R^2 = 0.936$, $P < 0.05$ *baseline compared to 50, 100, 200 and 400 g. Meals increased FI above baseline in a weight-dependant manner;* $R^2 = 0.994$, $P < 0.05$ *baseline compared to 200 and 400 g. During ad libitum intake, the AED algorithm detected 86% of all meals ≥15 g. Gastric distension reduced SWR and increased FI. Nitroglycerin reduced SWR. AED, using changes in FI and gastric SWR is feasible. Changes in FI and SWR are induced primarily by the presence of food in the stomach.*

Keywords *eating detection, effect of food, fundus impedance, slow waves, stomach.*

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INTRODUCTION

Food consumption is associated with predictable changes in gastric electromechanical activity. The pattern of periodic activity, the migrating motor complex, is interrupted and is replaced by a fed pattern of contractions.[1] During fasting, the proximal stomach maintains tone through vagal excitatory input and the myogenic property of fundic smooth muscle.[2] Food ingestion results in fundic relaxation, to receive and accommodate the food.[2,3] Food ingestion also predictably reduces the frequency of gastric slow waves.[4] In previous studies we observed that food ingestion consistently increases the resistance (impedance) between a pair of electrodes positioned in the fundus of dogs, and decreases the slow wave rate (SWR) recorded from the antrum.[5]

We hypothesized that these changes in gastric motor and electrical activity can be used to create an algorithm that can automatically detect the early phase of food consumption. A reliable way to detect meal initiation can be incorporated in therapies that are intended to interfere with food consumption, such as gastric electrical stimulation for obesity, or those that seek to ameliorate food-induced symptoms, as is the case in electrical stimulation for gastroparesis. Gastric electrical stimulation that is automatically timed to food ingestion and does not depend on patient input, may improve treatment efficacy and be more physiological than stimulation delivered in a continuous mode or at a pre-established schedule.

The aims of this study were to construct and test the performance of an algorithm for an automatic eating detection (AED) in a canine model.

MATERIALS AND METHODS

Animal preparation

Four female mongrel dogs (weight: 19.9 ± 0.5 kg) underwent gastric electrodes and recording device

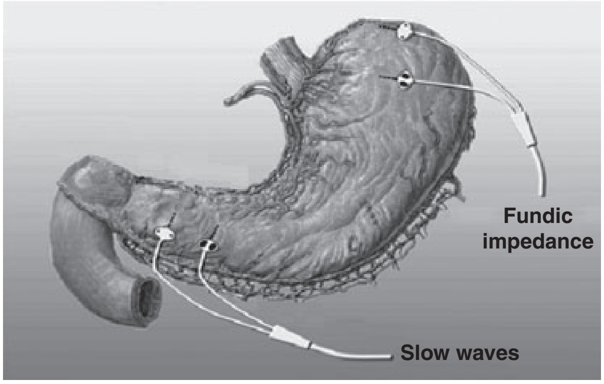

Figure 1 Electrode position in the stomach. This graphic represents the location of the bipolar electrodes and their use: the fundic electrodes were used to measure changes in impedance and the antral electrodes were used to record slow waves.

implantation. Anaesthesia was induced by administration of i.v. thiopental (Abbott Laboratories, Chicago, IL, USA) 20 mg kg^{-1}, and maintained by inhaled isoflurane (Abbott Laboratories), 1–2%. Via midline laparotomy, two bipolar electrodes (TIZER, MetaCure Inc., Orangeburg, NY, USA) were implanted in the seromuscular layer of the stomach in the following manner: one in the gastric fundus, 2 cm from gastro-oesophageal junction (GEJ), and one in the anterior wall of the antrum, 2 cm proximal from the pylorus (Fig. 1). The length of each electrode was 15 mm and each pair was placed 2.5 cm apart. The wires were brought out through the abdominal wall at the left flank. The electrodes were then connected to an implantable recording/stimulating device (TANTALUS^{TM}, Meta-Cure Inc.) located in a subcutaneous pocket, below the ribs, in the left abdominal flank. Thus, the device obtained continuous and simultaneous recordings of fundic impedance (FI) and gastric slow wave.

Signal recording

Data from simultaneous recordings of gastric SWs and FI were band-pass filtered (0.5–15 Hz) and sampled at a ra8te of 200 Hz and transmitted to an outside data logger (Shadow Logger, Metacure Inc.; 12 × 6 × 2 cm) via a radiofrequency wand (MetaCure, Inc., 8 cm diameter, 1.5 cm thick). Impedance was measured by delivery of a non-depolarizing stimulus at a frequency of 2.5 KHz, duration of 20 μs delivering a current of a few microamperes.

During experiments, a wand was positioned on the skin right above the implantable device, and was secured in place using an elastic bandage. The wand was connected to a battery-operated data logger that was located in an outside pocket of a vest that dogs wore during experiments. The vests (Lomir, Malone, NY, USA) protected the equipment, and facilitated the 24-h recording allowing the animals to move freely in their cages. Data obtained from these 24-h recordings were analysed using custom designed software in a portable laptop computer (series tablet PC keyboard; Hewlett-Packard, Korea).

Experiment 1: FI and SW changes to fixed-size meals

This experiment was undertaken to determine the effect of meal size on changes in FI and SWR. The data obtained were used to determine appropriate thresholds of FI and SWR that were incorporated in an AED that was tested when the dogs had free access to food (experiment 2).

Feeding regimen and signal recording Experiments started 3 weeks after the surgery, and after the dogs were trained to wear the wand and jacket. Changes in FI and SWR were assessed after 4 different meal sizes: 50, 100, 200 and 400 g of canned dog food (Science Diet, Hill's Pet Nutrition Inc., Topeka, KS, USA). We also tested the effect of a cephalic phase on FI and SWR by allowing dogs to see and smell the contents of 400 g of food for 3 min without them being able to eat it. Meals of different size were given in random order, on separate days. Each meal size was tested three times on separate days. All meals were consumed in the cages, after an overnight fast, under the supervision of one of the investigators. Thirty minutes after the cephalic phase test was performed or the test meal was consumed, dogs received the remaining meal to ensure appropriate daily intake.

Designing of an automatic eating detection algorithm

In the previous experiment, the SWR and the FI were observed to change in predictable directions during food intake. The magnitude of these changes is the basis for thresholds for detection. The eating detection algorithm was composed of two separate elements that would measure two aspects of gastric responses to food. An FI event would be defined by an increase in FI impedance level crossing a given threshold. An SWR event would be defined by a slow down in the SWR average, on a given number of consecutive events (typically 6), below baseline rate. In this algorithm, both thresholds should be crossed in a short-time window (10 min) to be considered an 'eating detection'.

Experiment 2: Testing AED algorithm performance during free access to food

This experiment was designed to test the performance of the selected thresholds while dogs had free access to food.

Feeding regimen and signal recording Continuous recording of changes in FI and SWs were obtained using the methodology described in the first experiment. Dogs were allowed to eat dog dry food (Science Diet, Hill's Pet Nutrition Inc.) *ad libitum* during 24-h periods. Food was provided in a bowl that was secured to a digital scale (scale and weighing indicator; CAS Corporation, East Rutherford, NJ, USA) located in each cage. These weighing systems were connected to a dedicated computer that recorded the input from each scale continuously. Scales were calibrated every 48 h. Scales were able to detect changes as small as 5 g. A standard amount of food (1800 g), about three times the usual daily intake (600 g), was placed in each bowl/ scale every morning. Digital scales continuously recorded the weight of the bowl for 24 h, allowing determination of when and how much food was consumed. Food-weight recordings were synchronized to gastric signals recordings (FI and SWs) obtained from each individual dog. All recordings were analysed to determine the beginning of food intake, its duration and the amount of food consumed in each occasion. These data were then correlated with simultaneous changes in FI and SWR, in this way, the performance of the algorithm for AED could be evaluated. Experiments were repeated six times in each dog.

Experiment 3: Effect of gastric mechanical distension and relaxation on fundic impedance and SWR

This experiment was conducted in a separate group of animals, to elucidate the mechanisms of food-induced changes in SWR and FI. Following a laparotomy, six healthy female mongrel dogs (weight: 29.1 ± 2.3 kg) underwent a sequence of acute studies, under general anaesthesia with thiopental (Abbott Laboratories) 20 mg kg^{-1}, i.v. and 1–2% inhaled isoflurane (Abbott Laboratories). One pair of temporary cardiac pacing electrodes (A&E Medical, Farmingdale, NJ, USA) was implanted in the gastric seromuscular gastric layer of the gastric fundus, 4 cm from the GEJ. These electrodes measured FI. Another pair of electrodes was implanted in the anterior antrum, for measurement of SWs. Electrodes in each pair were spaced 2 cm apart. Electrodes were connected to an external recording system (TANTALUS^{TM}, MetaCure Inc.). Continuous recording of SWs and FI were obtained using transcutaneous radiofrequency telemetry and a portable laptop computer (series tablet PC keyboard; Hewlett-Packard). Experiments were performed under general anaesthesia.

EXPERIMENTAL PROCEDURES

All dogs underwent two tests, performed in the same order, with continuous recording of FI and SW. Firstly, fundic balloon distension was performed using a polyethylene balloon with a maximum capacity of 800 mL (Mui Scientific, Mississauga, ON, Canada), inserted through the mouth. Each inflation was sustained for 5 min, and the balloon was completely deflated for 5 min in between. Balloon was filled with progressively increasing volumes: 50, 100, 200 and 400 mL. Fundic impedance during inflation was compared to 5 min of preceding baseline recording. At the end of this session, there was a pause of 20 min before another baseline of FI was obtained. Secondly, an i.v. infusion of nitroglycerin (Abbott Laboratories) was given for 10 min at a rate of 0.5 μg kg^{-1} min^{-1}.[6] SWR and FI recorded during nitroglycerin infusion were compared to values in the preceding baseline period. After completing all procedures, dogs were killed with an injection of Beuthanasia-D (pentobarbital + phenytoin, Schering Plough Animal Health) at a dose of 75 mg kg^{-1}, i.v.

The protocols were reviewed and accepted by the Institutional Animal Care and Use Committee at the Cleveland Clinic Foundation, Cleveland, OH, USA and at Cedars Sinai Medical Center, Los Angeles, CA, USA.

Analysis

Experiment 1 Data for each meal size, including the cephalic phase, were obtained three times per dog to account for variability. The mean value of each of the three meals was obtained in an off-line analysis of 24 h data, and the mean value of each of the three meals was used for analysis. Changes in SWR and FI were analysed for different size meals using linear correlation and ANOVA with repeat measures.

Experiment 2 Thresholds of SWR and FI were selected based on changes in these variables associated with 50 g meal in experiment 1. We chose this size because of the increase in FI and the significant decrease in SWR, compared to baseline, induced by this meal. These thresholds were used to test the performance of algorithm for AED. Analysis was carried out using the selected threshold for SWR and FI separately, and the combination.

Synchronized 24-h recordings of food weight and gastric signals were obtained on six separate days to account for differences in meal size. Data were analysed off-line for detected meals, meal weight and the duration of eating episodes. Algorithm performance was determined by matching the eating events detected by the algorithm with those detected by the synchronized digital scale. If the eating detection occurred up to 10 min from the beginning of the meal, it was considered a true event. If it occurred during other times it was considered a false positive. If the algorithm did not have a detection during the course of a meal it was considered a false negative. These variables were determined for SWR and FI alone and for the combination of FI and SWR. In addition, the percentage of the total food intake that was consumed during true positive AED was also measured.

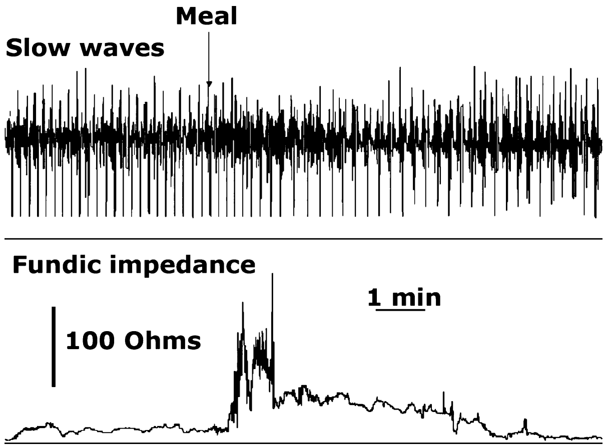

Figure 2 Changes in electromechanical gastric signals with meals. The upper panel shows the actual antral slow waves (SW) and the lower panel shows changes in fundic impedance (FI). Soon after meal initiation there is a marked increase in FI, and a clear increase in the time interval between consecutive SWs, indicating a reduction in SW's frequency. Maximum change in both variables is observed within the first few minutes after the meal. Fundic impedance increases after a meal and slowly returns to baseline values.

Experiment 3 The effect of balloon volume on SWR was presented as a percentage from baseline. The change in impedance was presented as a change from baselines in Ohms. Volume-related changes in these parameters were compared by ANOVA. Differences in SWR and FI between baseline and after nitroglycerin administration were analysed by a paired, two-tailed t-test. All data are given as mean ± SD, $P < 0.05$ for significance.

RESULTS

Experiment 1: FI and SW changes to fixed-volume meals

Typical responses of SWR and FI to a meal are depicted in Fig. 2. They are characterized by an almost immediate reduction in SWR and an increase in FI.

Effect of meal size on SWR The baseline SWR was 5.11 ± 0.13 cycles min^{-1}. Meal size correlated directly with reduction in SWR: the higher the weight the lower the SWR, $R^2 = 0.936$ (Table 1, Fig. 3). The

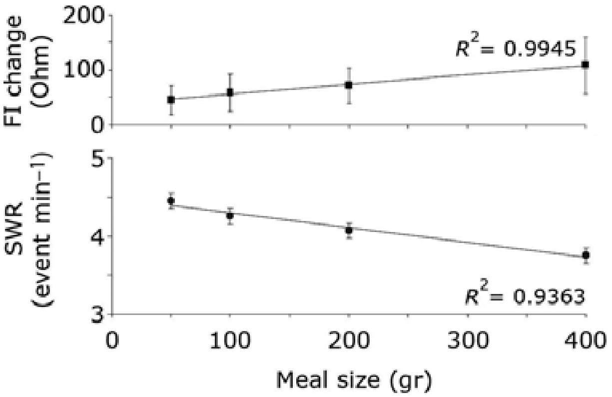

Figure 3 Effect of meal size on fundic impedance (FI; upper panel) and slow wave rate (SWR; lower panel). With increasing meal size, there is a linear increase in FI and a linear decrease in SWR.

Table 1 Effect of meal size on SWR

	Baseline	Cephalic	50 g	100 g	200 g	400 g
SWR (event min^{-1})	5.2 ± 0.1	4.7 ± 0.2	4.3 ± 0.3*	4.1 ± 0.7*	4.0 ± 0.3*	3.8 ± 0.1*
FI change (Ohms)	0	11.0 ± 4.0	47.5 ± 26.3	54.9 ± 26.9	71.5 ± 32.1‡	112.3 ± 43.0†‡

The effect of meals on SWR and FI (change above baseline) is volume dependent, the bigger the size of the meal the bigger the change.
Values are presented as mean ± SD.
*$P < 0.05$ when compared to baseline, ‡$P < 0.05$ when compared to baseline and to cephalic, †$P < 0.05$ when compared to 50 g.
FI, fundic impedance; SWR, slow wave rate.

decrease in SWR occurred within 2.05 ± 0.56 min after beginning the meal (Fig. 2).

Effect of meal size on FI Fundic impedance increased soon after starting the meal (Fig. 2), and increased as a function of meal weight, $R^2 = 0.994$ (Table 1, Fig. 3). The increase in FI peaked at 4.2 ± 1.1 min after beginning the meal.

Cephalic phase effect Seeing and smelling the food without swallowing caused a small decrease in SWR from a baseline of 5.2 ± 0.1 to 4.7 ± 0.2 cycles min^{-1} during cephalic phase (Table 1). There was also a minimal increase of 11.0 ± 4.0 Ohms in FI. Those changes were not statistically significant.

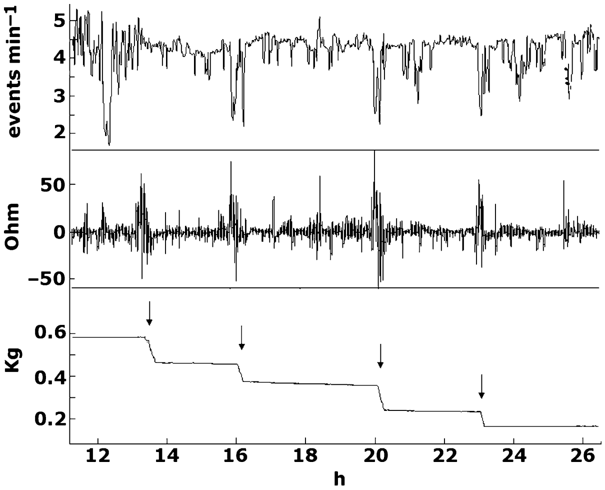

Figure 4 Simultaneous recordings of slow wave rate (SWR; upper panel), fundic impedance (FI; middle panel) and food weight (lower panel). This graphic represents an example from such recordings that lasted about 14 h. Each arrow in the lower panel represents a meal. Each meal, identified by a drop in food weight on the scale, caused a decrease in SWR, and an increase in FI. Some changes in these variables are not associated with meals, perhaps related to water ingestion.

Experiment 2: AED algorithm performance during free access to food

An example of recordings obtained during this experiment is illustrated in Fig. 4. For this experiment dogs were accustomed to *ad libitum* feeding, by providing an amount of food much larger than their usual daily intake. Dogs consumed an average of 4.3 ± 0.3 meals - day^{-1} for a total of 108 meals to be used for the algorithm testing. The average meal size was 120.6 ± 82.6 g and its duration was 12.1 ± 6.6 min. The duration of the meal correlated with the amount of food consumed, $R^2 = 0.65$, $P < 0.05$.

Results of the performance of the AED, using FI and SWR alone and in combination are shown in Table 2. The AED algorithm detected 86% of meals that weighed 15 g or more. We excluded meals of <15 g because there were few of them and also because they had a low caloric value. On average, the algorithm detected the meal 5.7 ± 2.6 min after its start. When changes in FI were used alone for AED, the sensitivity of the detection was similar to the combination of FI and SWR changes; however, the percentage of false positive increased almost by twofolds. Therefore, the addition of SWR changes to the AED algorithm increases the accuracy of the detection without affecting its sensitivity (Table 2). The AED algorithm detected 89.2 ± 6.3% of the total weight of food ingested. This suggests that most of the false negatives occurred with small meals.

Experiment 3: Effect of gastric mechanical distension and relaxation on fundic impedance and SWR

Modulation of slow wave rate Fundic distension caused a volume-dependent reduction in SWR. Values at each distension were compared to the preceding baseline. The per cent change in SWR during graded inflation, when compared to the preceding baseline was

Table 2 Performance of AED algorithm

		FI + SWR			FI			SWR		
Dogs	Meals	True +	False +	False −	True +	False +	False −	True +	False +	False −
1	23	22	6	1	20	14	3	11	68	12
2	27	22	4	5	25	10	2	11	66	16
3	24	19	11	5	24	15	0	7	72	17
4	34	30	7	4	30	8	4	27	62	7
Total (%)	100	86.1	23.1	13.9	91.7	32.2	8.3	51.9	82.7	48.1

Performance of the AED algorithm using thresholds of FI and SWR alone and in combination was displayed.
FI, fundic impedance; SWR, slow wave rate; AED, automatic eating detection.

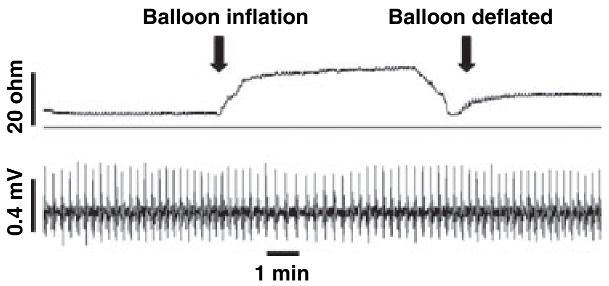

Figure 5 Effect of gastric balloon distension on slow wave rate (SWR; lower panel) and fundic impedance (FI; upper panel). Gastric distension with 400 mL caused a significant increase in a FI and a significant decrease in SWR as shown by the increase in the time interval between consecutive slow waves.

+3.9 ± 4.4% (50 mL), +2 ± 10.9% (100 mL), −15.2 ± 20.1% (200 mL) and −24.6 ± 12.4% (400 mL). A statistically significant decrease in SWR was seen only with the 400 mL distension.

Compared to control, nitroglycerin infusion consistently and significantly reduced SWR from 4.1 ± 0.6 to 3.8 ± 0.7 events min^{-1} ($P < 0.01$). The greatest reduction in SWR occurred within the first 5 min of the infusion (from 4.1 ± 0.6 to 3.7 ± 0.7 events min^{-1}, baseline *vs* nitroglycerin, respectively, $P < 0.01$); and the effect lasted for about 5 min after the infusion was stopped.

Modulation of fundic impedance Fundic distension with a balloon consistently increased FI. The increase over baseline impedance was 1.6 ± 1.3 (50 mL), 6.1 ± 5 (100 mL), 8.9 ± 7.1 (200 mL) and 19.2 ± 14.3 Ohms (400 mL). A statistically significant increase in FI was seen only with the 400 mL distension (Fig. 5).

Nitroglycerin infusion produced a consistent gradual increase in FI when compared to baseline, with a mean increase of 4.4 (1–7.9) Ohms, $P = 0.05$. The slow increase in FI with nitroglycerin reached a plateau within 4–6 min from the beginning of the infusion.

DISCUSSION

We found that food ingestion produces changes in FI and SWR that are consistent, distinct and predictable. Those changes can be used for automatic detection of food ingestion. This is a novel technique that may be useful in several clinical applications.

Our results show that FI increases right after meal initiation. Change is detectable with food intake of as little as 15 g, and values increase linearly as a function of meal size. Impedance increases are reliably detected when food is taken *ad libitum*. Our experiments suggest that food-induced increase in impedance is caused by both distension and relaxation of the fundus. The balloon-induced fundic distension increased FI in a volume-dependent manner, but a statistically significant increase was observed only with the larger volumes. The lack of statistically significant changes in FI seen with small volumes may be explained by the large capacity of the balloon we used (800 mL). Small volumes would have little effect on the shape of such large balloon, and should only minimally stretch the fundic wall. However, FI also increased with very small-volume meals (50 g in meal size experiment and 15 g in the *ad libitum* protocol). This too should cause only minimal stretching of fundic walls. This suggests that an increase in FI may also be caused by other mechanisms. One such mechanism may be active gastric relaxation. We observed a small increase in FI during the cephalic phase, when no food entered into the stomach. Cannon and Lieb were the first to describe fundus relaxation during sham feeding.[3] This receptive relaxation occurs during the early phase of meal intake and depends, in part, on vagally mediated reflexes induced by mechanical stimulation of the throat or distension of the oesophagus.[7–9] A second proximal stomach relaxation occurs during the accommodation reflex, or adaptive relaxation. It is mediated by the vagus and intrinsic nerves, once food enters the stomach.[10,11] Fundic relaxation is associated with release of NO, but other neurotransmitters, such as VIP, may also participate.[10,12–14] We simulated meal-induced fundus relaxation by intravascular infusion of nitroglycerin, an NO donor. This caused a small increase in FI. The contribution of active relaxation to changes in impedance is supported by a recent study by Simonian *et al.*[15] Using SPECT to measure gastric volume and emptying during meals, they showed that gastric volume increased significantly and very rapidly after food ingestion. They noticed that postprandial gastric volume was greater than what would be predicted by simply adding a volume of ingested food to the fasting gastric volume. This effect was most noticeable in the early postprandial phase.[15,16] Thus, we believe that the early increase in FI seen after meal initiation reflects two phenomena: a mechanical effect on the fundic wall by food entering into the gastric lumen, and an active gastric relaxation.

We found that meal initiation caused an early and consistent decrease in SWR that was directly correlated with the size of the meal. Food-induced slowing of SWR is also likely to be multifactorial in origin. Previous studies have shown that gastric distension diminishes SWR,[4] in a volume-dependent manner.[17,18] As with impedance, we observed that changes in SWR were correlated with balloon volume, but significantly diminished only with the largest volume. However, even small-volume meals decreased SWR, suggesting that the effect on SWR is not solely dependent on mechanical distension. Meal-induced changes in SWR are likely multifactorial in origin. Vagal stimulation increases SWR in the guinea-pigs antrum[19] as does a direct stretching of isolated gastric muscle.[20] Meal consumption, on the other hand, slows the rate of slow waves, suggesting that the presence of food in the stomach activate inhibitory mechanisms primarily. Hormones, paracrine substances and neurotransmitters can alter the rate of gastric slow wave generation. Acetylcholine, pentagastrin, carbachol, noradrenaline and CCK increase SWR in animal studies *in vivo* and *in vitro.*[21–23] On the other hand, agents that stimulate the production of cyclic nucleotides (such as nitric oxide donors), or inhibit their breakdown (such as cGMP phosphodiesterase inhibitors), decrease SWR.[24] In humans, both the proximal and distal stomach relax after ingestion of a meal.[25] Both cyclic AMP and cyclic GMP are involved in this gastric relaxation.[26] The effect of nitroglycerin on SWR in our study is consistent with the above observations, suggesting that *in vivo,* both mechanical distension and meal-induced activation of inhibitory neural pathways affect SWR. While the caloric content of the meal does modify SWR,[27] the changes in SWR that we observed occurred soon upon food ingestion, well before gastric contents are expected to enter the small bowel to elicit such effect.

We demonstrated that early changes in gastric electromechanical signals can be used for AED. Using this animal model, the AED detected 86% of all meals that weighed 15 or more grams. The meal detection occurred within 5–6 min from meal initiation and the frequency of missed events (false negatives) was low and seems to be related to small meals. The presence of false positives was low as well and may be explained in part by water intake, which was not controlled during this study. Therefore, this AED algorithm was able to detect most of the meals even when only a very small amount of food was ingested. A limitation of the study is the incorporation of repeat tests, carried out on different days in each dog. However, this was done because the weight of the meals in the *ad libitum* experiment was not standardized, and varied between meals and days. The activation of AED soon upon meal initiation and its low false-negative rate are important features for several possible clinical applications. There has been much interest lately in the use of gastric electrical stimulation as a treatment for obesity.[28–30] Such devices deliver GES continuously, without any meal cues. An effect on meal termination is likely to be better achieved when the stimulus is delivered in conjunction with the meal. Longer lifespan of the batteries and perhaps less habituation are also an advantage. Similar issues may be true in GES treatment for gastroparesis, where symptoms are commonly meal related.[31]

In conclusion AED, using specific changes in gastric electromechanical signals that occur very early after meal initiation, is feasible. This new technology has possible applications in the treatment of diseases that require implantable devices and an accurate identification of food intake.

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