Digestive Diseases and Sciences, Vol. 34, No. 10 (October 1989), pp. 1489–1493

Gastric Distension is a Physiologic Satiety Signal in the Dog

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Gastric distension is thought to produce satiety, but whether this effect is seen during physiologic distension by food is unknown. The purpose of this study was to determine whether levels of gastric distension seen during a meal have a satiety effect and whether the nutrient value of the meal was important. Four dogs were prepared with gastric, duodenal, and esophageal fistulas. Physiologic distension was determined by allowing the animals to eat liquid nutrient diet until sated and measuring the volume consumed and the time it took to consume it ($\bar{x}$ 2000 ml in 4 min). To test the effect of gastric distension on satiety, distension was produced during sham feeding by infusions of either liquid nutrient, inert liquid (Karaya), or by a water-filled balloon. Lower degrees of distension were also tested to determine if a dose–response relationship existed. Balloon, inert, and nutrient distension all inhibited sham feeding dose-dependently. Peak inhibitions of sham feeding caused by physiologic gastric distension (balloon, inert, nutrient) were 69 ± 5%, 67 ± 12%, and 61 ± 6%, respectively. In all cases, maximal distension terminated sham feeding before the end of the feeding period. The effect of gastric distension on feeding was not blocked by pretreatment with atropine (50 μg/kg). Thus, graded degrees of gastric distension, comparable to those seen during ingestion of a normal meal, produced graded inhibition of food intake by a noncholinergic mechanism and independent of the nutrient properties of the food.

KEY WORDS: sham feeding; atropine; gastric distension; satiety.

Signals from the brain and the upper gastrointestinal tract control appetite. That the brain controls the drive to eat is exemplified by true sham feeding (6). This central drive to eat can be modified by brain peptides (14). Gut satiety signals arise from the stomach and duodenum (5). Cholecystokinin (CCK) release from the duodenum and upper jejunum by food is thought to produce satiety (9), although this concept has been challenged recently. While gallbladder contraction and stimulation of pancreatic enzyme secretion are known to be physiologic actions of endogenously released CCK, termination of active feeding and production of satiety are probably not peripheral physiologic actions of the peptide (11).

Gastric distension occurs during feeding, although its importance as a satiety signal has not been clearly defined. To produce satiety, gastric distension must occur during active feeding and not be a preexisting condition (6). Since distension of any portion of the gastrointestinal tract during feeding can act as a noxious stimulus to terminate feeding (2), it is not known whether distension plays a physiologic role in the cessation of eating.

The purpose of this study was to quantitate the degree of distension that occurs normally during a

Manuscript received January 26, 1989; revised manuscript received May 23, 1989; accepted June 8, 1989.

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Supported in part by NIH grant R29-DK40790-01.

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0163-2116/89/1000-1489$06.00/0

meal in the dog and determine whether production of a similar degree of distension has an effect on sham feeding. In addition, we wished to determine whether the nutrient value of the distending material was important.

MATERIALS AND METHODS

Four mongrel dogs (20–30 kg) were prepared with gastric, duodenal, and chronic esophageal fistulas (10). The dogs were fed a liquid nutrient diet between studies, and all dogs were allowed one month recovery prior to study. Food, but not water, was withheld 24 hr prior to each study. All experiments were conducted at approximately the same time of day (1–4 PM).

Physiologic Gastric Distension during Feeding. The dogs were fed their liquid nutrient diet after a 24-hr fast and allowed to eat until sated. The volume consumed and the time it took to eat it were measured for each dog. In three separate tests for each dog, the meal was always finished within four minutes, and the average volume consumed was 2 liters.

Gastric Distension and Sham Feeding. In control studies a flaccid balloon was placed in the fundus of the stomach through the gastric fistula and the animals allowed to sham-feed for a period of 7.5 min without inflation of the balloon. In separate studies, during the first 4 min of sham feeding, the balloon was inflated to achieve the volume previously determined to be physiologic distension for each dog. Fifty and 25% increments of maximal distension were also tested for their effect on sham feeding.

We also studied the effect of graded volume distension with an inert liquid (2% Karaya) or nutrient liquid (blenderized food) on sham feeding. In each case the liquid was infused into the gastric fistula over 4 min at a rate that resulted in 100, 50, and 25% of maximal distension volumes.

Effect of Atropine on Distension-Induced Satiety. The dogs were allowed to sham-feed with and without inert gastric distension (50%). The effect of an intravenous bolus of atropine (50 μg/kg given 5 min before feeding) on distension-induced satiety was determined.

Materials. The gastric balloon was a modified condom tied to a catheter. The other end of the catheter was connected by tubing to a variable rheostat pump for infusion of water at the desired rate into the balloon. The balloon was placed in the fundus as follows: a string was passed down the esophageal fistula and out through the gastric fistula. The balloon was then attached to the string and pulled up to the fundus. The Karaya meal (Karaya powder, Hollister Co., Libertyville, Illinois) was prepared as a 2% (w/v) solution with distilled water. The blenderized diet used for studying the effect of distension with a nutrient meal on sham feeding was the same food the animals ate regularly and consisted of Kal Kan canned food (250 g, Kal Kan Foods, Vernon, California), Ensure (250 ml, Ross Laboratories, Columbus, Ohio), and 250 ml tap water.

Statistics. All data are expressed as $X \pm$ SEM. The sham feeding studies are expressed as milliliters of food consumed per minute (ml/min) during a 7.5-min feeding period. The time of sham-feed was determined to the nearest 30 sec. Significant differences between means were determined by Student's two-tailed paired t test when $P < 0.05$.

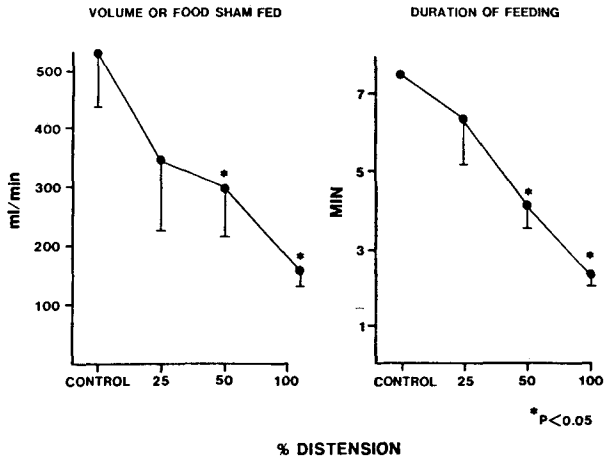

Fig 1. Effect of balloon gastric distension on sham feeding. The left panel shows the effect of graded amounts of gastric distension on the volume of food sham-fed during a 7.5-min test period. The right panel shows the effect of distension on the time that the animals sham-fed before they stopped. For the purpose of calculation, in the intact animal the volume of food ingested that produced satiety was considered to have caused 100% distension. Each point represents the mean ± SE of four experiments in four dogs. $*P < 0.05$ paired t test compared to zero distension.

RESULTS

The animals with the chronic esophageal fistula maintained their normal weight during the study period. Control studies were often repeated because normal eating behavior tended to vary from month to month. Gastric distension with any mode or volume used did not cause vomiting, retching, or any noticeable discomfort. Intragastric volume of inert liquid (Karaya) emptied very slowly through the pylorus, and approximately 90% of the instilled volumes were recovered from the gastric fistula at the end of the 7.5 min. Karaya was recovered from the stomach by gravity.

Gastric Distension and Sham Feeding. With an uninflated balloon in the stomach, the mean volume of food sham-fed was 535 ± 96 ml/min, and all animals ate for the entire 7.5 min. Graded increases in balloon gastric distension resulted in graded inhibition of sham feeding (Figure 1). Also, increasing gastric distension caused progressive shortening of the mean feeding time. Sham feeding stopped altogether in all animals with the 100% distension volume (Figure 1).

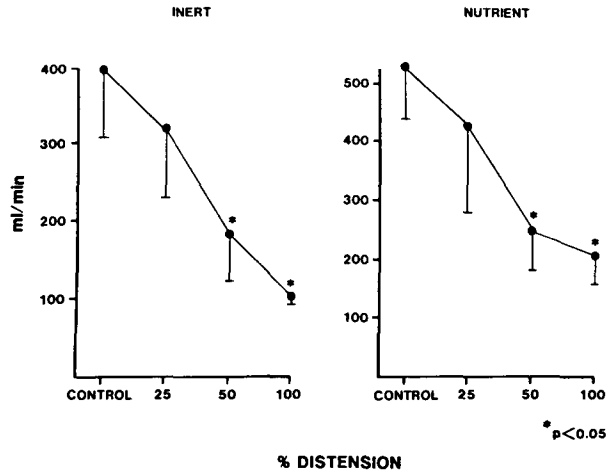

Fig 2. Effect of inert and nutrient gastric distension on sham feeding. The left panel shows the effect of graded volume of inert (2% Karaya) liquid on the volume of food sham-fed in a 7.5-min test period. The right panel shows the effect of nutrient (blenderized food) liquid on the volume of food sham-fed in a 7.5-min period. One hundred percent distension was determined in the intact animal as the volume of food ingested that produced satiety. Each point represents the mean ± SE of four experiments in four dogs. $*P < 0.05$ paired t test compared to zero distension. All data are expressed as milliters per minute.

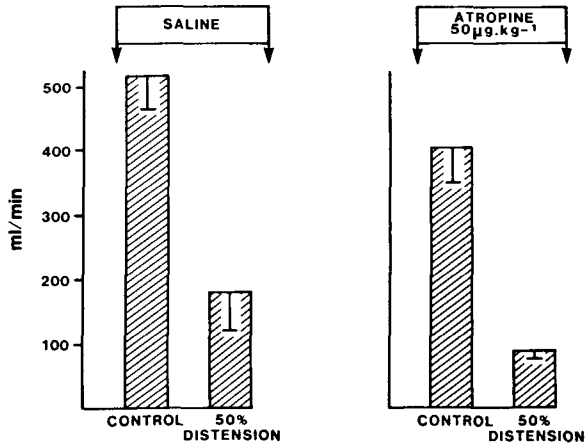

Fig 3. Effect of intravenous atropine on gastric distension induced satiety. The left bars show the effect of intravenous saline on distension-induced satiety. The right bars show the effect of intravenous atropine (50 μ/kg) given as a bolus 5 min prior to sham feeding. Control bars are the volumes of food sham-fed during the 7.5-min test period. Fifty percent distension bars are the sham feeding response to gastric distension with an inert liquid (2% Karaya). Fifty percent distension was defined in the intact animal as 50% of the volume of food ingested that produced satiety. $*P < 0.05$ paired t test compared to control.

Gastric distension with the inert or nutrient liquid meals caused similar inhibition of sham feeding. Distension with 25% of the meal volume caused a 29 ± 15% and 29 ± 20% inhibition in sham feeding for inert and nutrient distension, respectively. For the inert distension both the 50 and 100% distension volumes inhibited sham feeding by 57 ± 11% ($P < 0.05$) and 67 ± 12% ($P < 0.05$), respectively. Similarly, for the nutrient meal, both the 50 and 100% distension volumes significantly inhibited sham feeding by 40 ± 7% and 61 ± 6% ($P < 0.05$), respectively (Figure 2). Nutrient and inert liquid 100% distension stopped sham feeding in all animals prior to the end of the 7.5-min period.

Effect of Atropine on Distension-Induced Satiety. Control sham feeding without distension was 521 ± 54 ml/min. This was inhibited by 57 ± 11% during inert distension. In the dogs pretreated with atropine (50 μg/kg), the sham feeding rate was 409 ± 59 ml/min when no gastric distension was applied. In animals pretreated with atropine, distension produced 78 ± 6% inhibition of sham feeding (Figure 3).

DISCUSSION

This study demonstrates that levels of gastric distension that occur during the ingestion of a meal can produce satiety in the sham-feeding dogs. This effect was present despite the type of distension used: distension with balloon and inert nutrient meals all having similar effects. Atropine did not block distension-induced satiety; hence, the mechanism is not cholinergic. While there are extensive data to suggest that gastric distension acts as a peripheral satiety signal, this study is the first to establish that physiological levels of gastric distension (as occur during feeding, irrespective of the nutrient value of the meal) produce satiety.

Satiety signals can be divided into early and late. Early signals are those that stop active feeding, while late signals are those that maintain the state of satiety after the completion of feeding and determine the time interval between meals. Gastric distension is an early satiety signal. When gastric distension is introduced 5–40 min prior to, and maintained during, sham feeding, it does not produce satiety; but when the stomach is distended during sham feeding, the animal will stop feeding (6). The reason for these differences is unknown.

There has been a limited number of studies examining the effect of distension on sham feeding in the dog. Other than early experiments by Grossman and coworkers in the 1940s (6, 13), most studies have been on rats, and all indicate that gastric distension is a satiety signal. Pyloric obstruction and the resultant gastric distension during a meal

are sufficient to cause satiety with normal meal size (1, 7). Other studies have examined intestinal distension and its effect on eating behavior. Nonphysiologic distension of the intestinal tract has been studied and shown to cause nausea. A similar noxious stimulus causes nausea and vomiting in pathologic conditions, such as intestinal obstruction and necrotic bowel (2). It is important, therefore, to devise experiments in which distension is produced without causing noxious stimulation. We believe this objective was achieved in our experiments, since at no point did the animals retch or vomit.

Prior studies have stressed the importance of the caloric value of food and of gastric emptying in the regulation of feeding. Studies by McHugh and Moran (8) in monkeys implicate duodenal mechanisms, perhaps release of CCK, to delay gastric emptying and thereby cause gastric distension. It is not possible in such studies to distinguish between duodenal and gastric signals of satiety. Our studies with balloon distension show that a pure gastric stimulus can be a satiety signal. Furthermore, since our studies used a balloon, a nutrient meal, or a nonnutrient meal, the caloric value of the meal is of no importance in causing early satiety in this sham-feeding canine model. In a recent study, we have examined whether the effect of gastric distension on satiety is not potentiated by a "physiologic" dose of CCK (11). Doses of CCK that might be expected to mimic blood levels of the peptide seen after a meal had no effect on satiety when given alone and did not potentiate the effect of distension when the two stimuli were combined.

Our data suggest that the early satiety signal in the dog is entirely preduodenal. Satiety occurs very rapidly in the intact dog (within 2–3 min). In that length of the time very little food enters the duodenum (based on estimated rates of emptying of 0.08–0.24 kcal/min for dogs) (4). Therefore, during the time that a dog is completely sated, less than 1 kcal of nutrient has entered the duodenum. It is highly unlikely that duodenal factors would be important in the control of feeding during early satiety. Studies that examine the effect of intraduodenal nutrients on active feeding usually require much larger quantities to enter the duodenum prior to satiety (12). We have also demonstrated in other studies that intraduodenal sodium oleate sufficient to cause maximal gallbladder contraction and pancreatic protein secretion did not stop active feeding in the dog (11). Thus, in the dog, CCK is unlikely to be an important peripheral early signal of satiety.

The pathways that carry signals activated by gastric distension to satiety centers are not known. Atropine did not block the satiety effect of gastric distension. The dose chosen in this study (50 μg/kg) has been previously shown to block muscarinic activity in the dog stomach (3). In contrast, other studies have shown that vagotomized dogs lose their ability to control normal meal size (15). Taken together, the above findings suggest that noncholinergic vagal pathways mediate the effect of gastric distension on satiety.

In summary, we have shown that the gastric distension that occurs during the ingestion of a meal produces satiety by a noncholinergic mechanism. Early satiety in the dog appears to depend on gastric signals activated by distension. It is likely that postgastric signals are not important in the production of early satiety, but are likely to be important in determining the maintenance of the sated state between meals.

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