Cephalic phase of colonic pressure response to food

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Abstract
A cephalic phase of colonic pressure response to food was sought in five normal subjects (mean age 22.6 years, 22–24), studied on six separate occasions by recording intraluminal pressures in the unprepared sigmoid colon. Gastric acid secretion was measured simul-
taneously by continuous aspiration through a nasogastric tube. After a 60 minute basal period, one of five 30 minute food related cephalic stimuli; or a control stimulus was given in random order; records were continued for a further 120 minutes. The cephalic stimuli were: food discussion, sight and smell of food without taste, smell of food without sight or taste, sight of food without smell or taste, and modified sham feeding; the control stimulus was a discussion of neutral topics. Colonic pressures were expressed as study segment activity index (area under curve, mm Hg min) derived by fully automated computer analysis. Gastric acid output was expressed as mmol/30 min. Food discussion significantly (p<0.02, Wilcoxon’s rank sum test) increased colonic pressure activity compared with control or basal activity. Smell of food without sight or taste also significantly (p<0.03) increased the colonic pressure activity compared with control and basal periods. Sham feeding and sight and smell of food without taste significantly (p<0.02 and p<0.03) increased colonic pressures compared with control but not basal activity. The increase in colonic activity after sight of food without smell or taste was not significantly different from control or basal activity (p=0.44 and p=0.34). Food discussion was the strongest colonic stimulus tested. Food discussion and sham feeding significantly (p<0.02) stimulated gastric acid output above control and basal values. Sight and smell of food without taste significantly (p<0.02) increased acid output above basal. Smell of food without sight or taste and sight of food without smell or taste did not significantly (p=0.06, p=0.34) increase acid output. In contrast with the effect on colonic pressures, sham feeding was the best stimulus of acid output. Increased colonic pressure activity after food discussion correlated significantly (r=0.45, p<0.02) with gastric acid output. There was no correlation (r=−0.1, p=0.5) between colonic pressure activity and gastric acid output in the control study. These data show that there is a cephalic phase of the colonic response to food.

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Characterisation of neuronal, endocrine, and paracrine pathways that affect intraluminal pressures is important because abnormal colonic motility plays a part in irritable bowel syndrome, colonic diverticular disease, ulcerative colitis, and similar diseases. Colonic pressure responses may be mediated by a variety of pathways: neural, hormonal, and local reflexes may be involved. The main physiological stimulus for colonic segmenting pressures is the ingestion of food, but they are also affected by acute experimental stress and by drugs. It is generally thought that the colonic pressure response to eating is initiated by the local effect of nutrients or products of digestion on receptors in the mucosa of the upper digestive tract. Some of the possible mechanisms of the response, in particular the effect of calorie load and the constituents of meals, have been investigated by experimental studies in man.

The presence of a cephalic phase of colonic pressure response to food has never been formally investigated: on the contrary, its existence has been doubted. By contrast, the cephalic phase of gastric acid secretion is fully accepted and documented. Teleologically, the cephalic phase could be important in preparing the alimentary tract for receiving food when it is eventually swallowed. By analogy with the physiological mechanisms known to operate in the cephalic phase of gastric acid secretion, the hypothesis that a cephalic phase of the colonic pressure response to food exists was postulated, and tested experimentally in this study. Thought, sight, smell, sight and smell, and also sight and smell of food were used separately as candidate cephalic stimuli of the colonic pressure response to food.

The cephalic stimuli used in this study were derived from those developed by Feldman and Richardson for their studies of the cephalic phase of acid secretion. They systematically studied the relative importance of five food related cephalic stimuli: thought of food without sight or taste (food discussion), sight of food without smell or taste, smell of food without sight or taste, sight and smell of food without taste, and thought, sight, smell, and taste (sham feeding). A neutral cephalic stimulus, discussion about topics unrelated to food was used as a control. All food related cephalic stimuli significantly increased gastric acid output and serum gastrin concentrations. Modified sham feeding was the most potent agonist, followed by food discussion, sight and smell, sight alone, and smell alone. The neutral discussion did not change acid output or serum gastrin concentrations. These well researched cephalic stimuli of gastric acid secretion were tested with respect to their effect on colonic pressure activity.

Subjects
Five normal male volunteers (mean age 22.6 years, 22–24) were studied on six separate occasions. They had no history of gastro-
intestinal, anorectal, or metabolic disorder and all had a regular bowel habit. One subject was a regular smoker and all drank moderate amounts of alcohol. Informed consent was obtained from all subjects and the study was approved by the Brent Health Authority Ethical Committee.

Methods

QUESTIONNAIRE
All subjects completed a general questionnaire four weeks before the study which collected details of the subject’s day to day activities, dietary preferences, and bowel habit. Details of the subject’s favourite meal, hobbies, and general interests were also recorded. The questionnaire was very general so as not to disclose the aim of the study and to ensure that the subject’s attention was not focused on food. It provided the information necessary for the neutral, or control, discussion.

MEALS
Each subject’s favourite meal, derived from the questionnaire to ensure maximal cephalic effect, was prepared in advance in identical batches of five by high class professional caterers. The five meals for each subject were mass cooked and then divided into five servings, thus ensuring uniformity. The meals were prepared to a high standard, so that they could be presented in an attractive and appetising manner. The meals were deep frozen until needed for use. All the meals in a batch were and looked exactly the same. As none of the meals were eaten during the experiments, standardisation of the calorie, carbohydrate, protein, and fat content of the food between the five subjects was unnecessary.

INVESTIGATORS
The experimental protocol was too complex to be managed by one person. To ensure uniformity throughout the experiments each investigator had the same responsibilities in each study. One investigator (JR) performed all intubations, supervised the motility recording, and aspirated the gastric juice and was present in the laboratory at all times. Conversation with the subject was kept to a minimum and popular music was played to prevent boredom. The other investigator (AH) was responsible for the control and food discussions and for all the other cephalic stimuli and was present in the laboratory only during the stimulus periods.

STIMULI
Subjects were instructed to keep to their normal dietary routine during the study. They were not encouraged to attempt defaecation before fibre-optic flexible sigmoidoscopy. Each subject was studied the same time of day in the morning after fasting from midnight and five to seven days apart. Each cephalic stimulus was given on a separate day, in random order, after basal colonic pressure activity had been recorded for 60 minutes.

The stimuli were as follows:

Control discussion: thought of subject unrelated to food
The investigator conducting the interview entered the room and discussed a variety of neutral topics unrelated to food with the subject. Emotionally loaded subjects were not discussed.

Food discussion: thought of food without sight, smell or taste
The investigator discussed the subject’s favourite foods as detailed in the questionnaire. The subject was encouraged to talk about the food he liked, how he liked it prepared, and which restaurants served this food. He was asked to describe the smell, appearance, and the taste when eating his favourite meal. Care was taken to ensure that the subject did not see, smell, or taste food during the study, nor were food related topics mentioned during other periods of the study. The interviewer had no difficulty in maintaining the food discussion for the whole of the 30 minute period.

Sight only: sight of food without smell or taste
The subject’s favourite meal was reheated in a microwave oven in a kitchen remote from the laboratory, so that he could not hear, see, or smell the meal being cooked. It was presented at a normal distance from the subject in an attractive fashion with table cloth, cutlery, wine glass, and bottle of white wine on a decorated plate sealed with transparent film, so that no food odours could escape. The subject was asked to look and think about the food without discussion for 30 minutes, after which the meal was removed. Subjects were told at the time of presentation of the meal that they would be allowed to eat the meal at the end of the study.

Smell only: smell of food without sight or taste
The subject’s favourite meal was partly cooked by microwave oven in the kitchen remote from the laboratory and then brought into the laboratory concealed behind a screen, so the subject could hear and smell, but not see, the meal while it was fully reheated on a conventional hot plate. The meal was kept simmering for the 30 minute period of stimulation. The subject was asked to think about the smell of the food for this 30 minute period. After 30 minutes the meal and cooker were removed. The windows were opened and the room sprayed with a commercial air freshener to remove the conscious olfactory stimuli. Subjects were told that they would be allowed to eat the meal at the end of the study.

Sight and smell: sight and smell of food without taste
The subject’s favourite meal was partly reheated in the kitchen by microwave oven remote from the laboratory and then brought into the laboratory on the hot plate cooker so that the subject could see and smell the meal being cooked. The meal was simmered for 30 minutes and
the subject was encouraged to take part in the cooking by moving the food around on the hot plate of the cooker. The subject was asked to think about the food during this 30 minute period. After the stimulus period the meal and cooker were removed, the windows opened, and the room sprayed with air freshener. Subjects were told that they could eat the meal at the end of the study.

Sham feeding: ‘chew and spit’ modified sham feeding
A ‘chew and spit’ modified sham feeding techni-que was used over the whole 30 minute period, using the subject’s favourite meal. The subjects were encouraged to chew the food slowly and enjoy the taste of the meal, but not to swallow the food. Boluses of food were spat out into a container and covered by a layer of thick tissue so that the previously chewed bolus could not be seen by the subject. At the end of the 30 minute period the subject rinsed his mouth with cold water, which he then spit out. The windows of the room were then opened and the room sprayed with air freshener.

COLONIC PRESSURE ACTIVITY
The colon was intubated without bowel preparation with laxatives or enemas. The standard intubation technique using a flexible sigmoidoscope as described previously was used to place four manometric tubes into the descending, proximal sigmoid, distal sigmoid, and rectum 50, 40, 30, and 15 cm from the anus, respectively. Each tube was connected to a pressure transducer (Type P23ID, Statham, Hato Rey, PR, USA) and was perfused with distilled water at a constant rate of 0.25 ml/min using a pneumohydraulic pump (Mui Scientifique, Mississauga, Ontario, Canada). Pressures were recorded on a polygraph (Grass 7PD) calibrated at ambient temperature and pressure to 100 mm Hg cm⁻¹ by mercury manometer. The electrical signal driving each pen galvanometer was also passed to a custom built analogue to digital converter (PC-Polygraf, Synectics Medical, Sweden) and the digitised data stored on an IBM PC computer for automated analysis. A 30 minute rest period followed intubation before recordings were made. After a 60 minute basal period one of the cephalic stimuli was given to the subject for 30 minutes and pressure recordings were continued for a further 90 minutes.

ANALYSIS OF PRESSURE RECORDS
Pressure records were analysed by custom written fully automated computer analysis software (PC-Polygram, Gastrosoft, Sweden) in 10 minute periods. The main variable derived for analysis was the study segment activity index (mm Hg.min), as previously described in this laboratory. Synchronous hard copy records were also made on the polygraph. The details of pressure trace analysis and the design and validation of the computer system used have been fully described previously. Hard copy records were also visually analysed for segmental and propagative contractions.

GASTRIC ACID OUTPUT
Before the sigmoidoscopy, all the subjects were intubated transnasally with a 12 FG nasogastric tube and positioned in the gastric antrum under fluoroscopic control: the resting gastric contents were aspirated and discarded. Throughout the study gastric juice was continuously aspirated by manual syringe suction and collected in 15 minute aliquots. Subjects were encouraged to spit saliva onto tissue paper to prevent contaminating gastric juice.

The hydrogen ion concentration in the gastric aspirates was determined by titration against 0.1 M NaOH to pH 7.0 using an Autoburette system (Radiometer, Copenhagen, PHM62 – pH meter, TTT80 – Titrator, ABU80 – Autoburette, and TTA60 – Titration assembly). The Autoburette system was calibrated using reference pH buffers at pH 4.02 and 7.00 (Radiometer, Copenhagen). Gastric acid output was expressed in mmol H⁺/30 min.

Statistical analysis
The data pertaining to the colonic study segment activity index and to gastric acid output were analysed by comparisons with the control studies (control discussion) and also with the basal values of each study, using Wilcoxon’s signed rank test.

Results
Tables I and II show medians and ranges of colonic study segment activity index and gastric acid output, respectively.

<table>
<thead>
<tr>
<th>TABLE I Colonic study segment activity index</th>
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<tbody>
<tr>
<td>Colonic activity index (mm Hg.min)</td>
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<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>30 minute periods</td>
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<td>---------------------------------------------</td>
</tr>
<tr>
<td>Control</td>
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<tr>
<td>Food discussion</td>
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<tr>
<td>Sham feeding</td>
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<td>Sight only</td>
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<tr>
<td>Smell only</td>
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<tr>
<td>Sight and smell</td>
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</table>

* p<0.05 compared with control; † p<0.05 compared with basal.

<table>
<thead>
<tr>
<th>TABLE II Gastric acid output</th>
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<tbody>
<tr>
<td>Acid output (mmol H⁺/30 min)</td>
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<tr>
<td>---------------------------------------------</td>
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<tr>
<td>30 minute periods</td>
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<td>Control</td>
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<td>Sight and smell</td>
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</table>

* p<0.05 compared with control; † p<0.05 compared with basal.
CONTROL DISCUSSION
There was no significant change in colonic study segment activity index or in gastric acid output during, or after the control discussion (Figs 1 and 2), suggesting that the control discussion was a neutral cephalic stimulus to colonic pressure activity and gastric acid output.

FOOD DISCUSSION
Basal colonic pressure activity in the study segment during food discussion studies was not significantly (p=0.34) different from control. Food discussion produced an immediate and significant (p<0.02) increase in colonic study segment activity index above basal and control values which was maintained for the remainder of the study (Fig 1). Basal gastric acid output during food discussion studies was not significantly (p=0.22) different from control but increased significantly (p<0.02) during food discussion above basal and control values, returning to basal levels at the end of the stimulus period (Fig 2). Increased colonic pressure activity correlated significantly (r=0.45, p<0.02) with gastric acid output during food discussion (Fig 3) but not in the control study (r=−0.1, p>0.5).

MODIFIED SHAM FEEDING
Basal colonic pressure activity during sham feeding was not different from control (p=0.34). Modified sham feeding significantly (p<0.02) increased colonic study segment activity index during the stimulus and the after stimulus periods compared with control, but not with basal periods (p=0.25; Fig 4). Basal gastric acid output during sham feeding studies was not different (p=0.34) from control. Modified sham feeding significantly (p<0.02) increased acid secretion above control and basal outputs, and this was sustained for 90 minutes after the sham feeding stimulus (Fig 5).

SIGHT ONLY
Basal pressure data during sight only studies were not different from control (p=0.34). The sight only stimulus did not increase colonic study segment activity index in comparison with control (p=0.44) or basal (p=0.34) periods. Basal gastric acid output during sight only studies was not (p=0.89) different from control, and this stimulus did not increase gastric acid output in comparison with either control (p=0.25) or basal (p=0.06) periods.

SMELL ONLY
Basal colonic pressure activity during smell only studies was not different from control (p=0.17). The smell only stimulus significantly increased colonic study segment activity index compared with control (p<0.02) and basal (p<0.03) data. Basal gastric acid output during smell only studies was not different from control (p=0.22). In contrast with the results of colonic activity, the increase in acid output which occurred during the smell only stimulus was not signific-

TABLE III  Quantitative pressure data from pressure trace (Fig 6). Basal and food discussion 30 minute periods

<table>
<thead>
<tr>
<th>Channel 1 50 cm</th>
<th>Channel 2 40 cm</th>
<th>Channel 3 30 cm</th>
<th>Channel 4 15 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal Food discussion</td>
<td>Basal Food discussion</td>
<td>Basal Food discussion</td>
<td>Basal Food discussion</td>
</tr>
<tr>
<td>Basal</td>
<td>111-1</td>
<td>258-8</td>
<td>150-8</td>
</tr>
<tr>
<td>Mean pressure (mm Hg)</td>
<td>7-4</td>
<td>54-8</td>
<td>27-7</td>
</tr>
<tr>
<td>Activity index (mm Hg min)</td>
<td>222</td>
<td>1656</td>
<td>831</td>
</tr>
</tbody>
</table>
Cephalic phase of colonic pressure response to food

SIGHT AND SMELL
Basal colonic pressure activity during sight and smell studies was not different from control (p=0.25). Colonic study segment activity index increased significantly (p=0.03) above control data during the 30 minute period following the stimulus. There was no increase (p=0.11), however, in colonic activity index above basal during the stimulus or, after stimulus periods. During the basal periods gastric acid output was not significantly (p=0.89) different from control.

QUALITATIVE ANALYSIS OF COLONIC PRESSURE RECORDS
The increased colonic activity index during the food discussion stimulus was associated with a number of qualitative changes in colonic pressure activity as illustrated in Figure 6, which shows the 4 channel pressure trace for the 30 minute periods before (top) and during food discussion (bottom). There was a predominance of segmental contractions throughout the study in both the basal and food discussion periods. No propagating contractions or rectal motor complexes were seen. During food discussion there was a qualitative increase in segmental activity in all channels associated with quantitative increases in maximum amplitude, mean amplitude, and activity index (Table III). There was no change in the baseline pressure to account for the quantitative increases in pressure activity seen during food discussion.

Discussion
The existence of a cephalic phase of the colonic response to food was sought for and found in this study, which further investigated the relative potency of thought, sight, smell, and taste of food as agonists in this reflex. The hypothesis that a cephalic phase of colonic response to food may exist was suggested by previous observations in this laboratory, which indicated that the colonic response was synchronous with the start of the meal, that significantly increased colonic pressures occurred during sham feeding, and that the colonic response was affected by the route of administration of the meal.11

Procedures in this study followed the model developed by Feldman and Richardson11 for the investigation of the cephalic phase of gastric acid secretion. The present experiments conducted under similar conditions showed that discussion of food, a pure cephalic stimulus, significantly increased colonic pressure activity and stimulated gastric acid secretion, confirming the previous studies. The increased colonic pressure activity was the result of stimulation of segmenting contractions, without any evidence of propulsive wave forms. Control discussion which was not food related and devoid of emotional content, did not alter colonic pressure activity or gastric acid secretion.

Food discussion was the most potent stimulus of colonic pressure activity. The other pure cephalic stimuli – sight, smell, and sight and smell – were less potent as stimulants of colonic pressure activity. Their effectiveness, expressed as a percentage of the response to food discussion, was 51% for sight, 71% for smell, and 66% for sight and smell. The reasons for these variations must remain conjectural at present. It may be noteworthy, however, that food discussion required the subject’s complete concentration and participation during the 30 minute stimulus period. In the case of the sight, smell, and sight and smell stimuli the concen-
Sham feeding increased colonic pressures and produced the greatest increase in gastric acid output, which persisted into the after stimulus observation period. This was probably because particles of food, which were seen in gastric aspirates, were inadvertently swallowed by the subjects despite all reasonable precautions. In our hands therefore, this stimulus cannot be considered purely cephalic in nature. The colonic response to sham feeding, which was only 52% of that to food discussion, may have been modulated by the presence of food in the stomach. The relative potencies of the other cephalic stimuli in terms of gastric acid output expressed as a percentage of the response to sham feeding were remarkably similar to those reported by Feldman and Richardson.1 Mean responses in this study (their results in parenthesis) were: 66% (66%) for food discussion, 39% (33%) for sight and smell, 29% (28%) for sight only, and 32% (23%) with smell only.

Acid was continuously aspirated in our experiments, and although it is unlikely that the aspiration was entirely complete, transepithelial losses were probably very small. Thus, the influence of cephalically stimulated acid secretion on more distal gut motor function, including that of the large intestine, needs to be determined. Further studies in our laboratory indicate that the entry of acid into the duodenum does not influence the cephalic motor stimulation of the colon.15 Adherence to a rigid time frame and the administration of the stimuli in random order were adopted to minimise bias because of the possible habituation of the subjects to the conditions of the study or to circadian variations in gut function.13-16

Studies of the relation between the central nervous system and the colon have mainly been concerned with the effects of acute experimental stress17-19 or of sleep.13-14 The present data show another aspect of the way in which the central nervous system can modulate the function of the distal large intestine. The pathways through which this effect is mediated is unclear. The vagus mediates the gastric cephalic response1 but there is no direct evidence that the vagus mediates the cephalic colonic response. Although anatomical dissection limits the distribution of this nerve to the proximal two thirds of the colon,20 there is physiological evidence that a neural mechanism plays a part in the distal colonic motor responses to food,21 which is present in patients with complete transection of the spinal cord.22 On the other hand, recent studies in primates suggests that the vagus innervates the whole colon.23 Interestingly, the small intestine seems to be unaffected by cephalic influences24 despite the well documented differences in small intestinal motility between the fed and fasted states.

Results of this study show the existence of a cephalic phase of the colonic pressure response to food in healthy subjects. The pathways involved in the mediation of the response remain to be determined.
Some of the data were presented to the British Society of Gastroenterology, Sheffield, September 1988.

Our thanks are due to Ms Annie O’Dell of ‘Hotstuff’ for her expert cookery. This work was funded by a project grant from the Medical Research Council.


8 Feldman M, Richardson CT. Role of thought, sight, smell, and taste of food in the cephalic phase of gastric acid secretion in humans. *Gastroenterology* 1986; 90: 428–35.


