MRI assessment of the postprandial gastrointestinal motility and peptide response in healthy humans

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Abstract
Background: Feeding triggers inter-related gastrointestinal (GI) motor, peptide and appetite responses. These are rarely studied together due to methodological limitations. Recent MRI advances allow pan-intestinal, non-invasive assessment of motility in the undisturbed gut.

This study aimed to develop a methodology to assess pan-intestinal motility and transit in a single session using MRI and compare imaging findings to GI peptide responses to a test meal and symptoms in a healthy volunteer cohort.

Methods: Fifteen healthy volunteers (29.3±2.7 years and BMI 20.1±1.2 kg m⁻²) underwent baseline and postprandial MRI scans, symptom questionnaires, and blood sampling (for subsequent GI peptide analysis, Glucagon-like peptide-1 [GLP-1], Polypeptide YY [PYY], Cholecystokinin [CCK]) at intervals for 270 minutes following a 400 g soup meal (204 kcal, Heinz, UK). Gastric volume, gall bladder volume, small bowel water content, small bowel motility, and whole gut transit were measured from the MRI scans.

Key Results: (mean±SEM) Small bowel motility index increased from fasting 39±3 arbitrary units (a.u.) to a maximum of 87±7 a.u. immediately after feeding. PYY increased from fasting 98±10 pg mL⁻¹ to 149±14 pg mL⁻¹ at 30 minutes and GLP-1 from fasting 15±3 μg mL⁻¹ to 22±4 μg mL⁻¹. CCK increased from fasting 0.40±0.06 pmol mL⁻¹ to 0.94±0.1 pmol mL⁻¹. Gastric volumes declined with a T₁/₂ of 46±5 minute and the gallbladder contracted from a fasting volume of 19±2 mL to 12±2 mL. Small bowel water content increased from 39±2 mL⁻¹ to 51±2 mL⁻¹ postprandial. Fullness VAS score increased from 9±5 mm to 41±6 mm at 30 minutes postprandial.

Conclusions and Inferences: The test meal challenge was effective in inducing a change in MRI motility end-points which will improve understanding of the pathophysiological postprandial GI response.

Keywords
bowel, gastrointestinal motility, gut peptides, MRI, satiety
1 | INTRODUCTION

The clinical relevance of measuring intestinal motility has been recently shown through its correlation with intestinal inflammation in Crohn’s disease.1,2

MRI methodology has recently come to the fore offering repeatable means to measure global and segmental motility.3 Furthermore, MR does not expose the subject to ionizing radiation, permitting serial scanning4-6 which is commonly indicated in chronic intestinal disorders.

Abdominal pain represents a predominant symptom both in functional and organic intestinal diseases and commonly occurs in the postprandial state rather than after a prolonged fast. Feeding triggers a range of gastrointestinal (GI) responses such as motility and secretion of fluid and hormones. Postprandial GI motility is stimulated by luminal distention and is modulated by luminal nutrients. Enteroendocrine cells react to the luminal contents by releasing a variety of gastrointestinal peptides like Cholecystokinin (CCK), Peptide YY (PYY) and Glucagon-like peptide 1 (GLP-1).7 CCK delays gastric emptying and stimulates gall bladder contraction,8 PYY slows meal transit through a delay in gastric emptying and increasing the GI transit time (known as ileal brake),9 while GLP-1 delays gastric emptying10 and decreases small bowel motility separately.11,12

It thus comes as rather a major diagnostic limitation that most investigative MR paradigms are undertaken in the fasting patient and not in the physiological state with an abnormally distended bowel with contrast agent. Advances in the availability of MRI scanners, increases in the speed of acquisition and growing acceptance of this method for the investigation gastrointestinal disease has driven its role in the GI physiology. A number of techniques to assess fasting motility in a fasted and prepared during an MR enterography (MRE) are now available13 enabling rapid, reproducible, and sensitive assessment of global and segmental motility to complement morphological changes seen through structural imaging.14,15

In this study, we aim to develop a methodology to assess pan-intestinal motility assessment in a single session using MRI in a fed and physiological state and to compare imaging findings to postprandial GI peptide responses and key patient symptoms in a healthy volunteer’s cohort. This work will serve as a platform to enhance our understanding of GI physiology and diagnostic capabilities in relevant disease groups.

2 | MATERIALS AND METHODS

2.1 | Subjects

This study was approved by the local Ethics Committee of the University of Nottingham (H19062014). This study is registered on clinical trials.gov with identifier NCT02717117. All participants gave informed written consent.

Healthy volunteers (median age 26 [range 19-50] years, BMI mean 20±1 kg m⁻²) were recruited from the local campus population. Participants with a history of inflammatory bowel disease, smokers,16 a history of bowel resections or any gastrointestinal surgery, history of pancreatic insufficiency, thyroid disease, diabetes, protein-pump inhibitor usage or any medication that affects gastric emptying or small bowel transit and any potential participants scoring very highly on the depression scale questionnaire were excluded. Standard MRI exclusion criteria were applied.

2.2 | Test meal

The test meal consisted of: cream of chicken soup (400 g) (or mushroom for vegetarians) (Heinz, Wigan, UK), chosen, respectively, by 6 and 9 participants. The nutrient content of this meal/100 g was: energy (kcal) 51, protein 1.5 g (1.5%), carbohydrate 4.7 g (4.5%), fat 2.9 g (2.9%). This meal has been previously shown to reliably induce a GI peptide response.17,18

2.3 | Study design

This study was open label. MRI marker capsules were used to measure whole gut transit time.19 Participants were given five MRI marker capsules (20 mm×7 mm) filled with 0.4 mL⁻¹ 15 μmol L⁻¹ Gadoteric acid, an MRI contrast agent, to take home. They were instructed to swallow these 24 hour before attending the unit for their study day and undergoing the baseline MRI scans as previously described.19 They were asked to fill in a questionnaire to ensure adherence to the study day restrictions.

The subjects were asked to fast from 2000 hour the previous evening and to avoid alcohol, caffeine, strenuous exercise and any medication that could affect gut function for 18 hour before the experiment (Figure S1).
On the day of the scan, Participants attended the 1.5 T Philips Achieva MRI scanner (Philips Healthcare, Best, the Netherlands) at the Sir Peter Mansfield Imaging Centre (SPMIC) at the University Park Campus, University of Nottingham. Participants were cannulated at arrival (0800) and underwent a baseline fasting scan at 0900 hours (defined at t=−20 minutes time point), together with a fasting baseline blood sample. The 60 minutes interval between cannulation and acquisition of baseline measurements was introduced to allow the subjects to normalize to a baseline calm physiological state. At 0925 hours, they were asked to consume all their test meal in a quiet lounge next to the scanner within a maximum time of 20 minutes so that at 0945 hours the subjects underwent a first immediate postprandial scan (defined as t=0 min).

This was followed with data collection (MRI, questionnaire data and 10 mL−1 blood samples) time points every 15 minutes for the first 60 minutes and then every 30 minutes up to 270 minutes. Blood samples were collected by a research nurse. The first 2 mL−1 of each sample was discarded to avoid contamination with the saline used to maintain patency. Blood was collected into vacutainer tubes containing 0.325 mL−1 of aprotinin, (Trasylol, Bayer) (Dorset, England).

At each time point, the MRI procedures took approximately 15 minutes, including subject positioning on the scanner bed, setup of the MRI scans and data collection. For the first 60 minutes the subjects were kept inside the scanner. After this the subjects were kept sitting upright in a quiet lounge next to the scanner for the rest of the study day except for the subsequent MRI acquisitions. At each time point, they filled a 100 mm Visual analogue scale (VAS) symptoms questionnaire scoring their feeling of fullness, bloating, distension, abdominal pain/discomfort and nausea. The VAS anchors are from ’not’ to ’extremely’. At the end of the 270 minutes healthy volunteers were allowed to leave.

## Magnetic resonance imaging

MRI scanning was carried out supine. Participants were scanned using a range of sequences. At each time point scans were acquired to assess gastric volume, gall bladder volume, small bowel water content and small bowel motility. In addition at baseline the position of the MRI marker capsules were determined to measure whole gut transit time.

Gastric emptying was assessed using a balanced gradient echo sequence (bTFE) acquiring 50 contiguous axial slices with reconstructed in-plane resolution 2.0×1.77 mm2, slice thickness 5 mm and 0 mm slice gap, echo time (TE)=1.5 ms, repetition time (TR)=3.0 ms, flip angle 80°, SENSE 2.0 within one breath hold of ~16 seconds. This imaging sequence yields good contrast between the stomach contents and other abdominal organs. Samples containing mobile water appear brighter than viscous samples with reduced water content and mobility.

The content of apparent freely mobile water in the small bowel was assessed as previously described using a single-shot fast spin echo sequence acquiring 24 contiguous coronal slices with reconstructed in-plane resolution 0.78×0.78 mm2, slice thickness 7 mm and slice gap 0mm, TE=320 ms, TR=8000 ms, SPIR fat saturation within one breath hold of 24 seconds. This sequence yields high-intensity signals from areas with freely mobile fluid and dark signals from poorly mobile or bound water and all other body tissues.

Small bowel motility was assessed using a single slice cine-MRI acquisition set at six contiguous parallel coronal planes through the small bowel. Data were acquired using a balanced gradient echo sequence (bTFE) with reconstructed in-plane resolution 1.49×1.7 mm2, echo time (TE)=1.52 ms, repetition time (TR)=3.0 ms, flip angle 80°, SENSE 2.0 at a repetition time of 1 image per second for a duration of 1 minute for each plane with gentle free breathing throughout the acquisition.

Whole gut transit was assessed using two different Coronal 3D T1 weighted turbo field echo (TFE) sequences. Each comprised two separate stacks with a 30 mm overlap, acquired on two separate breath holds. Firstly a T1 weighted 3D TFE sequence with SPAIR fat saturation. Sequence parameters for each station were as follows: TE=1.9 ms, TR=4.0 ms, FA=10°, FOV=250×398×160 mm3. Acquired resolution 2.3×2.3×5 mm3, reconstructed to 1.4×1.4×2.5 mm3, with a 288×288 reconstructed matrix. 64 slices were acquired with a half-scan factor of 0.7 in the phase direction and 0.85 in the slice direction in a 23 seconds breath hold. The second sequence, another T1-weighted 3D TFE sequence with a 2-echo readout and mDIXON reconstruction of the water only images was acquired with increased resolution using SENSE and 36 maximum intensity projection (MIP) images were generated from this data to create a 3D view of the colon to aid in defining the position of the capsules. Imaging parameters at each station were as follows: TE1/TE2=1.4/2.5 ms, TR=3.8 ms, FA=10°, FOV=250×371×200 mm3. Acquired resolution 1.8×1.8×3.6 mm3, reconstructed to 1.0×1.0×1.8 mm3, with a 384×384 reconstructed matrix. 111 slices were acquired with a SENSE factor of 2.0 in the phase direction in a 22 seconds breath hold.

Gall bladder volume was measured pre- and postprandial, at every acquisition time point up to 60 minutes postprandially. This was carried out using the same images as for the gastric volumes as previously shown.

## Plasma collection and peptides assays analysis

On the morning of the test, 0.325 mL−1 of aprotinin was added to vacutainer tubes (BD-361017, BD Diagnostics, Oxford) for collection for each time point aiming for a final volume of 6.5 mL−1. Fasting 10 mL−1 blood sample was drawn and collected in the tubes. After the test meal, data were acquired every 15 minutes for the first 60 minutes and every 30 minutes thereafter to 270 minutes. Twelve samples were taken totalling 120 mL−1. Samples were centrifuged at 3000 rpm for 10 minutes and stored on ice. Plasma peptides (total GLP-1, total PYY) were analysed through enzyme-linked immunosorbent assay (ELISA) techniques (Millipore, UK) as previously shown. The concentrations of serum CCK were measured by radioimmunoassay (RIA) (Euro Diagnostic Products, Sweden) as previously shown.
2.6 | Data analysis

2.6.1 | Motility assessment

All dynamic data were processed with Dual Registration of Abdominal Motion (DRAM) (Motilent, Ford, UK). DRAM first removes respiratory motion before applying the optic flow registration as previously described by Odille et al. to correct local deformation caused by bowel wall motion and model intensity changes caused by luminal flow. Registration results were further analysed using a customized graphical user interface written in MATLAB (MathWorks, Natick, MA, USA).

Published methods of assessing small bowel motility have been applied in Magnetic Resonance Enterography (MRE). MRE involves distending the bowel lumen with a large volume of luminal contrast medium, which stimulates wall movement and facilitates at the same time the registration process. The aim of our project was to measure motility in a physiological state after a nutrient meal rather than an artificially distended state. Since postprandial small bowel motility does not produce the same motion or appearance of the lumen as in MRE, a different approach to assessing the small bowel motility was required. The technique used in this study quantified the motility of the bowel using the pixel signal changes through the time series, within a defined region of interest (ROI) placed over the small bowel loops. The metric was calculated as follows:

For each pixel in the registered dataset, a power spectrum of the intensity changes across the time series (smoothed using a running average of 5 pixels to reduce noise) was calculated and then summed across all frequencies. This metric was termed the total power, and reflected bowel motility, both in terms of segmental oscillations and bolus movement of contents, typically seen postprandially.

Two independent observers (AK, CH) drew ROIs manually over all the loops of the small bowel in all the slices for each imaging datasets (Figure 1). From these ROIs the mean total power across all small bowel pixels was calculated. A larger total power motility index represents higher small bowel motility.

2.6.2 | Small bowel water content (SBWC)

SBWC was measured as previously validated, using in house software written in IDL (Research Systems Inc. Boulder, Colorado, USA).

Briefly, this method assumed that any pixel with signal intensity above the calculated threshold in the heavily T2-weighted coronal images is filled with free water. Structures such as blood vessels, bladder, and gall bladder are manually excluded.

2.6.3 | Gall bladder and gastric volumes

Gall bladder and gastric volumes were quantified using in house software written in IDL (Research Systems Inc. Boulder, Colorado, USA). This method uses a semiautomatic previously validated thresholding region growing technique to define the content of the stomach and gas within the stomach on each image slice.

For total gastric volume was calculated as the sum of the stomach contents and any gas. Postprandial gastric content volumes were fitted to a 5 parameter equation to model the emptying process and allow the calculation of the gastric half-emptying time ($T_{1/2}$).

2.6.4 | Whole gut transit (WGT)

Whole gut transit was assessed as previously described. From the two sets of MRI images a transit score was calculated by subdividing the bowel into eight sections and each capsule was scored according to its position in the colon at 24 hours. A weighting factor was calculated for each capsule depending on the difference of the capsule score from the median capsule score.

2.6.5 | Visual analogue scale (VAS)

Symptoms regarding appetite, satiety and abdominal pain were scored at each time point using previously validated questionnaire.

2.7 | Statistical analyses

Due to the pilot nature of this study, it was not possible to power it but similar studies done by our group have used similar-sized cohorts. The data are expressed as mean±standard error of the mean (SEM). Normality of the data was assessed using Shapiro-Wilk’s test. One-way analysis of variance (ANOVA) was used to assess the significance of differences. When the analysis of variance was
significant, post hoc test assessments of the individual time points were performed using the Dunnett’s for parametric data or Dunn’s test for non-parametric data, to account for multiple comparisons. All statistical analyses were performed using GraphPad Prism 7.01 (La Jolla, USA). A P-value less than .05 was considered statistically significant.

3 | RESULTS

All fifteen healthy volunteers (9 female, 6 male, age 29.3±2.7 years and BMI 20.1±1.2 kg m⁻²) completed the study and tolerated the experimental procedures well without any adverse event.

3.1 | Gallbladder volumes

The changes in gallbladder volumes with time are shown in Figure S2. This demonstrated a moderate and significant postprandial decrease in the volume from 19±2 mL⁻¹ (mean±SEM) at baseline to 12±2 mL⁻¹ immediately postprandial t=0 min (P≤.0001).

3.2 | Gastric volumes

The baseline gastric volumes showed small amount of resting gastric juices of 26±7 mL⁻¹. Gastric content volumes rose significantly upon feeding to 418±17 mL⁻¹ at t=0 (P≤.0001) after which the volume of the stomach declined and went back to baseline (37±7 mL⁻¹) at 150 minutes with an average time to empty half of the stomach contents (T₁/₂) of 46±5 minute (Figure 2).

3.3 | Small bowel motility

From Figure 3 it can be seen that the motility index increased significantly from fasting 39±3 arbitrary units (a.u.) to a maximum of 87±7 a.u. immediately postprandial (t=0 minute) (P≤.001) after feeding and then gradually decreased back to around baseline (44±4 a.u.) in 90 minutes. Motility index rose slightly again at 120 minutes to 55±4 a.u. and decreased back again to 38±4 a.u. at 240 minutes.

3.4 | Small bowel water content

The data in Figure 4 shows a small amount of fasting (t=−20 minutes) small bowel water content of 39±2 mL⁻¹. The test meal induced a significant change in small bowel water content. Immediately, after the all soup meal was ingested, this increases to a maximum of 51±2 mL⁻¹ (P≤.05) at 15 minutes. The volume decreased toward baseline (38±2 mL⁻¹) at 60 minutes after which a second peak at 180 minutes is clearly seen with a volume of 65±3 mL⁻¹.

3.5 | Whole gut transit

The median average weighted position score (WAPS) of the MRI capsules was 1.0 (0-3.8). As described previously,¹⁵ the WAPS at 24 hours was converted to WGT in hours, giving a median of 33 hours.
3.6 | Total GLP-1

The meal induced significant postprandial changes in plasma measures of total GLP-1 (P≤.01). The mean GLP-1 data (Figure 5) from healthy volunteers showed a postprandial peak from fasting volume of 15±3 μg mL⁻¹ to 22±4 μg mL⁻¹ (t=0 minute). The GLP-1 levels dropped (12±3 μg mL⁻¹) after 30 minutes and remained around baseline levels for the rest of the study day.

3.7 | Total PYY

PYY (Figure 6) increased significantly (P≤.001) from fasting 98±10 pg mL⁻¹ to 149±14 pg mL⁻¹ at 30 minutes postprandially in healthy volunteers. PYY returned to baseline after 2 hours postprandially and later dropped even further to reach 71±13 pg mL⁻¹ at 270 minutes.

3.8 | CCK

Plasma CCK levels (Figure 7) increased significantly (P≤.01) from fasting 0.40±0.06 pmol mL⁻¹ to 0.94±0.1 pmol mL⁻¹ at t=30 minutes and then steadily decreased after 60 minutes to reach baseline (0.4±0.01 pmol mL⁻¹) for the rest of the study day.

3.9 | Symptom VAS data

The meal induced a significant increase in fullness. VAS increased from 9±5 to 44±5 at 0 minute and 41±6 at 30 minutes postprandial (P<.001). The feeling returned to baseline thereafter. Bloating, distention, pain, and nausea did not change significantly. (Table 1).

4 | DISCUSSION

The test meal challenge was effective in inducing a change in multiple physiological quantified end-points and in monitoring markers of GI motility in a single MRI study session which was acceptable to the subjects. To our knowledge this is the first study measuring gut motility in an undisturbed bowel after a nutrient meal without artificially distending the bowel.

The physiological parameters measured in this study were in the expected range for a normal healthy cohort as we have shown repeatedly in our previous studies.28-30

The test meal was ingested within a maximum of 20 minutes by the 15 subjects and hence acted as a food bolus in the stomach. The meal itself was richer in carbohydrate content (4.5%) and fat (2.9%) rather than protein (1.5%) and hence would be a good stimulus for GLP-1, PYY and CCK secretion by the enteroendocrine L cells and I cells respectively.

The meal used for this experimental work was a homogenous soup rather than a solid meal. T1/2 for the gastric emptying was 57±5 minute starting off with a maximal volume of 458±20 mL⁻¹. The gastric emptying was approximately linear from 0 minute to 90 minutes postprandial. This finding is similar to our previous observations whereby following a solid meal with a drink, there is an initial rapid gastric
emptying of the liquid drink in the first 0 to 75 minutes postprandial, followed by slower phase of emptying of the solid food. The mean reported fullness VAS increased from 9.0 in the fasting state to 44 immediately postprandial, with a decline to baseline within ~180 minutes. This rapid gastric emptying had an effect on the GI peptide responses to the test meal, changes in small bowel water content and the small bowel motility. In this work we once again observed a bimodal peak in small bowel water content in the postprandial state up to 270 minutes. The subjects’ mean fasting baseline small bowel water content was 39±2 mL\(^{-1}\), increasing to a maximum of 51±2 mL\(^{-1}\). The volume decreased towards baseline (38±2 mL\(^{-1}\)) at 60 minutes in an early ‘gastric phase’ after which a second peak at 180 minutes was clearly seen with a volume of 65±3 mL\(^{-1}\), otherwise known as a later ‘intestinal phase.’ The early drop observed is probably representative of absorption of water and available nutrients (sucrose and glucose) which are co-transported with sodium and water following the resulting osmotic gradient across the intestinal mucosa. This net absorption together with an activated postprandial gastro-ileal reflex causing emptying of the contents of the distal ileum into the ascending colon, lead to a decrease in small bowel water content. The second peak or intestinal phase is due to an increase in pancreatico-biliary and enterocyte secretion.

The plasma levels of GLP-1 increased rapidly from 15±3 ug mL\(^{-1}\) to 22±4 ug mL\(^{-1}\) in response to the carbohydrate load within the meal. It is known that one of the principal factors governing gastric emptying is the total carbohydrate load, which through proximal duodenal absorption of simple digestible carbohydrates leads to an increase in GLP-1 secretion and a delay in gastric emptying. The level of CCK usually increases 10-30 minutes after food intake\(^6\) as was confirmed in this study. In a parallel, gall bladder contraction occurred within 20 minutes of meal ingestion which would explain the 50% decrease in gall bladder volume.

In this work, we measured motility of the unprepared small bowel in response to a nutrient test meal for the first time. Mean motility peaked at 87±7 a.u. immediately postprandial. The early increase may be due to the fact that large boluses of meal move rapidly through the duodenum and upper jejunum increasing the volume amount of small bowel associated with the motion per unit of intestinal fluid volume present. Moreover, a prompt gastro-ileo reflux would facilitate emptying of the distal small bowel content into the ascending colon. The small bowel motility decreased back to baseline at approximately 90 minutes, when the emptying of the stomach has almost completed. This decrease coincided with maximal plasma levels of GLP-1 and PYY\(^{33}\), which have previously been associated with delayed small bowel transit. Mean small bowel motility once again peaked at 120 minutes. There could be multiple possible explanations for this change. Between 90 and 120 minutes, mean plasma levels of PYY and GLP-1 dropped back to preprandial levels hence minimizing their negative effect on small bowel motility. At a similar time period small bowel water content increased due to an increased in intestinal and pancreatico-biliary secretions. Such a small bowel distention could make small bowel motility more apparent and easier to measure or otherwise be a stimulus itself for smooth muscle contraction. To our knowledge, this is the first time that such detailed and non-invasive assessment of small bowel physiology has ever been described in the postprandial state with MRI. The whole gut transit time reported in this study was a median of 33 hours. This is comparable to our previous reports of 31 hours using the same methodology.\(^{19}\)

There are limitations in the study. The meal used was small in both volume and caloric intake, hence providing a submaximal stimulus to the GI tract. We chose this meal, due to its known effects on GI peptide response and because it could be tolerated in an otherwise sick patient population and could be administered safely and in a timely fashion in a clinical setting. Despite this postprandial physiological changes have been observed both in MR measures, patient symptoms and GI peptides. The age range 19-50 years was broad though we would not expect major differences in GI motility within this range.

In this study we have established an unprecedented platform for measuring postprandial small bowel motility in human subjects using MRI, and correlated this to known physiological GI peptide

| Time point | Fullness | Bloating | Distention | Pain/discomfort | Nausea/sickness |
|------------|---------|----------|------------|----------------|----------------|
| -20        | 9±5     | 7±3      | 4±2        | 1±1            | 6±4            |
| 0          | 44±5**  | 9±3      | 4±2        | 0±0            | 2±2            |
| 15         | 41±6*   | 10±3     | 5±3        | 0±0            | 2±2            |
| 30         | 41±6**  | 6±3      | 3±2        | 0±0            | 1±1            |
| 45         | 37±7    | 7±3      | 3±2        | 0±0            | 1±1            |
| 60         | 31±7    | 5±3      | 2±2        | 0±0            | 1±1            |
| 90         | 26±6    | 5±3      | 3±3        | 0±0            | 0±0            |
| 120        | 20±6    | 7±4      | 3±2        | 0±0            | 1±1            |
| 150        | 13±4    | 4±2      | 1±1        | 0±0            | 0±0            |
| 180        | 12±5    | 2±1      | 1±1        | 0±0            | 0±0            |
| 210        | 7±4     | 1±1      | 1±1        | 0±0            | 0±0            |
| 240        | 5±2     | 0±0      | 1±1        | 0±0            | 0±0            |
| 270        | 3±1     | 0±0      | 0±0        | 0±0            | 0±0            |

**P≤.001 and *P<.05 vs baseline value.
responses and symptoms. This work shows that such methodology exists and feasible. The length of our study is such that it may be difficult to implement in a busy clinical setting as is, though one could choose to scan only during the early postprandial time where the response is maximal. Presently intestinal motility had only been measured in the fasting state or on a bowel prepared with large volumes of luminal contrast, which may be less relevant to some of the postprandial symptoms experienced by patients. Mapping out such postprandial physiological changes in disease groups will allow us to understand patient symptoms better and perhaps identify GI peptides as possible biomarkers of dysmotility and patient symptoms attributing to a poor quality of life. Further future work may be able to normalize such dysmotility through commercially available GI peptide inhibitors

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DISCLOSURE

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AUTHOR CONTRIBUTIONS

AK, CLH, LM, and GWM designed the research. AK, AN recruited the patients. AK collected the data. AK, AM, CLH, ML, YF, GS, and SP analysed the data. AK, CLH, LM, and GWM wrote the manuscript draft. All authors revised the final manuscript.

REFERENCES

1. Menys A, Atkinson D, Odille F, et al. Quantified terminal ileal motility during MR enterography as a potential biomarker of Crohn’s disease activity: a preliminary study. Eur Radiol. 2012;22:2494-2501.

2. Menys A, Helbren E, Makanyanga J, et al. Small bowel strictures in Crohn’s disease: a quantitative investigation of intestinal motility using MR enterography. Neurogastroen Motil. 2013;25:967-e775.

3. Plumb AA, Menys A, Russo E, et al. Magnetic resonance imaging-quantified small bowel motility is a sensitive marker of response to medical therapy in Crohn’s disease. Aliment Phar Therap. 2015;42:343-355.

4. Knuesel PR, Kubik RA, Crook DW, Eigenmann F, Froehlich JM. Assessment of dynamic contrast enhancement of the small bowel in active Crohn’s disease using 3D MR enterography. Eur J Radiol. 2010;73:607-613.

5. Cronin CG, Lohan DG, Browne AM, Alhajeri AN, Roche C, Murphy JM. MR enterography in the evaluation of small bowel dilation. Clin Radiol. 2009;64:1026-1034.

6. Fidler JL, Guimaraes L, Einstein DM. MR imaging of the small bowel. Radiographics. 2009;29:1811-1826.

7. Bruen CM, O’Halloran F, Cashman KD, Giblin L. The effects of food components on hormonal signalling in gastrointestinal enteroendocrine cells. Food Funct. 2012;3:1131-1143.

8. Huda MSB, Wilding JPH, Pinkney JH. Gut peptides and the regulation of appetite. Obes Rev. 2006;7:163-182.

9. Batterham RL, Cohen MA, Ellis SM, et al. Inhibition of food intake in obese subjects by peptide YY3-36. New Engl J Med. 2003;349:941-948.

10. Little TJ, Pilichiewicz AN, Russo E, et al. Effects of intravenous glucagon-like peptide-1 on gastric emptying and intragastric distribution in healthy subjects: relationships with postprandial glycemic and insulimic responses. J Clin Endocr Metab. 2006;91:1916-1923.

11. Schirra J, Nicolaus M, Roggel R, et al. Endogenous glucagon-like peptide 1 controls entodocrine pancreatic secretion and antro-pyloroduodenal motility in humans. Gut. 2006;55:243-251.

12. Horsthuis K, Bipat S, Bennink R, Stoker J. Inflammatory bowel disease diagnosed with US, MR, scintigraphy, and CT: meta-analysis of prospective studies. Radiology. 2008;247:64-79.

13. Bickelhaupt S, Pazahr R, Chuck N, et al. Crohn’s disease: small bowel motility impairment correlates with inflammatory-related markers C-reactive protein and calprotectin. Neurogastroen Motil. 2013;25:467-473.

14. Odille F, Menys A, Ahmed A, Punwani S, Taylor SA, Atkinson D. Quantitative assessment of small bowel motility by nonrigid registration of dynamic MR images. Magn Reson Med. 2012;68:783-793.

15. Menys A, Taylor SA, Emmanuel A, et al. Global small bowel motility: assessment with dynamic MR imaging. Radiology. 2013;269:442-449.

16. Kadota K, Takeshima F, Inoue K, et al. Effects of smoking cessation on gastric emptying in smokers. J Clin Gastroenterol. 2010;44:e71-e75.

17. Moran GW, Leslie FC, McLaughlin JT. Crohn’s disease affecting the small bowel is associated with reduced appetite and elevated levels of circulating gut peptides. Clin Nutr. 2013;32:404-411.

18. Leslie FC, Thompson DG, McLaughlin JT, Varro A, Dockray GJ, Mandal BK. Plasma cholecystokinin concentrations are elevated in acute upper gastrointestinal infections. QJM Int J Med. 2003;96:870-871.

19. Chaddock G, Lom C, Hoad CL, et al. Novel MRI tests of orocecal transit time and whole gut transit time: studies in normal subjects. Neurogastroen Motil. 2014;26:205-214.

20. Hoad CL, Parker H, Hudders N, et al. Measurement of gastric meal and secretion volumes using magnetic resonance imaging. Phys Med Biol. 2015;60:1367-1383.

21. Marciani L, Cox EF, Hoad CL, et al. Effects of various food ingredients on gall bladder emptying. Eur J Clin Nutr. 2013;67:1182-1187.

22. Hoad CL, Marciani L, Foley S, et al. Non-invasive quantification of small bowel water content by MRI: a validation study. Phys Med Biol. 2007;52:6909-6922.

23. Eggers H, Brendel B, Dujindam A, Herigault G. Dual-echo dixon imaging with flexible choice of echo times. Magn Reson Med. 2011;65:96-107.

24. Astbury NM, Taylor MA, Macdonald IA. Breakfast consumption affects appetite, energy intake, and the metabolic and endocrine responses to foods consumed later in the day in male habitual breakfast eaters. J Nutr. 2011;141:1381-1389.

25. Hamy V, Dikaios N, Punwani S, et al. Respiratory motion correction in dynamic MRI using robust data decomposition registration - application to DCE-MRI. Med Image Anal. 2014;18:301-313.

26. Silverthorn DU. Human Physiology: An Integrated APPROACH. London: Pearson; 2012.

27. Parker HL, Tucker E, Hoad CL, et al. Development and validation of a large, modular test meal with liquid and solid components for
assessment of gastric motor and sensory function by non-invasive imaging. Neurogastroenterol Motil. 2016;28:554-568.

28. Marciani L, Cox EF, Hoad CL, et al. Postprandial changes in small bowel water content in healthy subjects and patients with irritable bowel syndrome. Gastroenterology. 2010;138:469-477, 477 e1.

29. Marciani L, Pritchard SE, Hellier-Woods C, et al. Delayed gastric emptying and reduced postprandial small bowel water content of equi-caloric whole meal bread versus rice meals in healthy subjects: novel MRI insights. Eur J Clin Nutr. 2013;67:754-758.

30. Marciani L, Hall N, Pritchard SE, et al. Preventing gastric sieving by blending a solid/water meal enhances satiation in healthy humans. J Nutr. 2012;142:1253-1258.

31. Kellum JM, Albuquerque FC, Stoner MC, Harris RP. Stroking human jejunal mucosa induces 5-HT release and Cl- secretion via afferent neurons and 5-HT4 receptors. Am J Physiol. 1999;277:G515-G520.

32. Gentilcore D, Nair NS, Vanis L, et al. Comparative effects of oral and intraduodenal glucose on blood pressure, heart rate, and splanchnic blood flow in healthy older subjects. Am J Physiol Regul Integr Comp Physiol. 2009;297:R716-R722.

33. Pironi L, Stanghellini V, Miglioli M, et al. Fat-induced ileal brake in humans - a dose-dependent phenomenon correlated to the plasma-levels of peptide-Yy. Gastroenterology. 1993;105:733-739.

34. Marathe CS, Rayner CK, Jones KL, Horowitz M. Effects of GLP-1 and incretin-based therapies on gastrointestinal motor function. Exp Diabetes Res. 2011;2011:1-10.

35. Edelbroek M, Horowitz M, Dent J, et al. Effects of duodenal distention on fasting and postprandial antropyloroduodenal motility in humans. Gastroenterology. 1994;106:583-592.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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