HHS Public Access

Author manuscript

Neurogastroenterol Motil. Author manuscript; available in PMC 2016 February 03.

Published in final edited form as:

Neurogastroenterol Motil. 2014 May ; 26(5): 696–704. doi:10.1111/nmo.12318.

Motility Response to Colonic Distention is Increased in Post-infectious Irritable Bowel Syndrome (PI-IBS)

Motoyori Kanazawa[1,2], **Olafur S. Palsson**[1], **Miranda A.L. van Tilburg**[1], **Lisa M. Gangarosa**[1], **Shin Fukudo**[2], and **William E. Whitehead.**[1]

[1]Center for Functional GI and Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill, Campus Box 7555, Chapel Hill, NC 27599-7555, USA

[2]Department of Behavioral Medicine, Tohoku University Graduate School of Medicine, 2-1 Seiryo, Aoba, Sendai 980-8575, Japan

Abstract

Background—Acute intestinal infection leads to persistent intestinal smooth muscle hypercontractility and pain hypersensitivity after resolution of the infection in animal models. We investigated whether post-infectious irritable bowel syndrome (PI-IBS) is associated with abnormalities in phasic contractions of the colon, smooth muscle tone and pain sensitivity compared to non-PI-IBS (NI-IBS) or healthy controls (HC).

Methods—218 Rome III positive IBS patients and 43 healthy controls participated. IBS patients were designated PI-IBS if their IBS symptoms began following an episode of gastroenteritis characterized by 2 or more of: fever, vomiting, or diarrhea. Pain threshold to phasic distentions of the descending colon was assessed using a barostat. Colonic motility was assessed with the barostat bag minimally inflated to the individual operating pressure (IOP), at 20 mmHg above the IOP, and following a test meal. IBS symptom severity and psychological symptoms were assessed by the IBS Severity Scale (IBS-SS) and the Brief Symptom Inventory-18 (BSI-18).

Key Results—Twenty-two (10.1%) met criteria for PI-IBS. Both IBS and HC groups showed a significant increase in motility index during intraluminal distention and following meals. The magnitude of the response to distention above (orad to) the balloon was significantly greater in PI-IBS compared with NI-IBS ($p<0.05$) or HC ($p<0.01$). Differences between PI-IBS and NI-IBS were not significant for IBS symptom severity, pain threshold, barostat bag volumes, or any psychological score on the BSI-18.

Address for correspondence: Motoyori Kanazawa, MD, PhD., Department of Behavioral Medicine, Tohoku University Graduate School of Medicine, 2-1 Seiryo, Aoba, Sendai 980-8575, Japan. Phone & Fax: +81-22-717-7655, m-kanazawa@med.tohoku.ac.jp.

DISCLOSURE

No competing interests declared.

AUTHOR CONTRIBUTION

WEW: the guarantor of this paper, and he participated in study design, data collection, data analysis, and manuscript preparation. MK: participated in study design, data analysis, and preparation of the manuscript. OSP: participated in study design and data analysis. MALVT: participated in data collection and data analysis. LMG: participated in data collection. SF: participated in data analysis and manuscript preparation.

Conclusions & Inferences—Patients with PI-IBS have greater colonic hypercontractility than NI-IBS. We speculate that sustained mild mucosal inflammation may cause this colonic irritability.

Keywords

irritable bowel syndrome (IBS); gut inflammation; colonic motility; visceral sensitivity

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by frequent abdominal pain accompanied by diarrhea or constipation. These symptoms are thought to be due to gut motor hyper-reactivity and enhanced visceral pain sensitivity [1]. Psychosocial factors have also been implicated in the clinical expression of IBS [2]. A newly recognized risk factor for IBS is infectious gastroenteritis [3–9].

Most people with food or water borne gastrointestinal infections recover completely following resolution of the acute infection, but a significant proportion (3.7–36%) go on to develop chronic gastrointestinal symptoms consistent with IBS and these patients are designated as having post-infectious IBS (PI-IBS) [3]. The most common causative agents identified to date are *Salmonella*, *Shigella*, and *Campylobacter* [7–9], and the predominant bowel pattern noted is diarrhea predominant IBS (IBS-D) [7].

Several studies have evaluated risk factors for the development or maintenance of PI-IBS and identified female gender, psychological symptoms, and elevated levels of inflammatory markers as significantly associated with PI-IBS [3]: First, females were shown to be at higher risk for PI-IBS in multiple studies [7–9]. Second, two studies addressed the role of psychological symptoms but came to different conclusions. In one study, patients with PI-IBS showed higher scores for anxiety and depression compared with individuals who had no IBS symptoms 3 months following acute infection [7], whereas another study failed to identify anxiety or depression as an independent predictor of PI-IBS [10]. Third, a mild transient gut inflammation led to long-term change of visceral hypersensitivity in an animal model of PI-IBS [11]. In another animal study, persistent intestinal smooth muscle hypercontractility was present after resolution of chemically induced inflammation [12]. It has been reported that colonic transit is accelerated in patients with PI-IBS compared to controls [13], but differences in phasic colon motility and smooth muscle tone have not been studied in humans with PI-IBS. Last of all, PI-IBS patients show increased numbers of inflammatory cells and 5HT-containing enterochromaffin (EC) cells in the rectal mucosa [7, 14, 15], increased gut permeability [14, 15] and increased sensitivity to rectal distention [13, 16] compared to control subjects.

Thus, except for psychological symptoms, there are consistent findings in humans for the role of other risk factors for PI-IBS. The aims of this study were to investigate whether PI-IBS is associated with abnormalities in phasic contractions of the colon, smooth muscle tone, pain sensitivity, bowel symptoms, or psychological symptoms compared to IBS patients with a non-infectious etiology for IBS (NI-IBS) and healthy controls.

MATERIALS AND METHODS

Subjects

A preliminary report on this study was published in 2008 [17], which described the test procedures for the assessment of phasic motility, muscle tone, pain sensitivity, and psychological symptoms. The aims of the 2008 publication were to describe the contribution of pain sensitivity, colon motility, smooth muscle tone, and psychological symptoms to the severity of IBS symptoms and altered bowel habits. PI-IBS patients were not separated out from other IBS patients in that report, which described data for 129 of IBS patients and 30 of healthy subjects included in the current analysis.

Subjects were recruited by advertisements or physician referrals and screened by telephone. The study population consisted of 258 patients with a prior physician diagnosis of IBS who fulfilled Rome III criteria for IBS [18] and had current IBS symptoms (abdominal pain or discomfort at least one-fourth of the time in the last 3 months). Exclusion criteria were a history of gastrointestinal surgery (other than appendectomy or cholecystectomy), inflammatory bowel disease, celiac disease, lactose malabsorption, heart disease or diabetes mellitus, and pregnant or suffering from any acute infectious disease at the time of study.

According to bowel habit reported by patients, patients were classified by Rome III guidelines [18] into three subgroups: IBS-D defined as loose (mushy) or watery stool ≥25% and hard or lumpy stool <25% of bowel movements, IBS-C defined as hard or lumpy stool ≥25% and loose or watery stools <25% of bowel movements, and IBS-mixed (IBS-M) defined as loose or watery stools ≥25% of the time plus hard or lumpy stools ≥25% of the time.

PI-IBS was defined by retrospective questionnaire as the acute onset of new IBS symptoms in an individual who had not previously met the Rome criteria for IBS, if they reported 2 or more of the following symptoms immediately following an acute illness: fever, vomiting, diarrhea, or a positive bacterial stool culture according to the previous report [19]. Forty of 258 patients with IBS were excluded because they responded “unknown” to the question on whether IBS symptoms were preceded by infectious gastroenteritis.

The control population consisted of 43 subjects with no recurring gastrointestinal symptoms. Exclusion criteria for controls were average stool frequency of less than 3/week or more than 3/day, abdominal pain, or use of a laxative or anti-diarrheal agent on more than two occasions over the prior year, history of alcohol or substance abuse, a psychiatric diagnosis, or any of the medical conditions listed above for the IBS patients. The study was approved by the Institutional Review Board of the University of North Carolina (UNC), and all subjects provided written informed consent.

Study Design

Subjects were admitted to the General Clinical Research Center at the University of North Carolina for a 24–30 hour period. They were asked to fast for at least 4 hours prior to reporting for testing. On the day of admission, the study nurse took a medical history and performed a physical examination, and the findings were reviewed by study physicians to

ascertain whether the participants were eligible for the study. After screening for eligibility, the following questionnaires were completed: The Irritable Bowel Syndrome Severity Scale (IBS-SSS) [20], the IBS-QOL [21, 22], and the Brief Symptom Inventory-18 (BSI-18) [23]. A low fiber meal was consumed at approximately 5:00 pm. Day 1 ended with a bowel cleanout consisting of 1.5 oz of Fleet's phosphosoda consumed at 6:00 pm and repeated at 9:00 pm.

Colonic Sensory and Motility Testing

All physiological testing was performed on day 2 according to the protocol shown in Figure 1. On the morning of day 2 at approximately 8:00 AM, the barostat catheter was placed into the descending colon by sigmoidoscope. Following catheter placement, the subject rested for 90 min before testing began. The *motility catheter* (Model C7-CB-0026, Mui Scientific Mississauga, Ontario, Canada) is 5 mm in outside diameter. It includes four small catheters used to measure pressures 2.5 and 5 cm from the proximal and distal edges of the bag. A 10 cm long, 600 mL capacity polyethylene bag (Model CT-BP600R, Mui Scientific) was attached to the surface of the motility catheter and tied with surgical thread. The *barostat* is a computer-controlled pump (Distender II model, G&J Electronics, Willowdale, Ontario, Canada) used for testing sensory thresholds and smooth muscle tone in the lumen of the bowel. The *pneumohydraulic pump* (eight-channel hydraulic capillary infusion system, Arndorfer Inc, Greendale, WI) uses a tank of compressed air to force degassed sterile water from a reservoir through four capillary (very small diameter) catheters that are connected to four pressure transducers. Sample distentions were then performed during which the barostat bag was inflated in a stepwise fashion by increasing bag pressure by 4 mmHg every 15 seconds until the subject reported moderate pain (rating of 3 on a 0–5 scale). The sample distentions served three purposes: (1) to insure that the barostat bag was unfolded; (2) to teach the subject how to use the rating scale to describe the intensity of colonic sensations; and (3) to decrease anticipatory anxiety. The barostat bag was then slowly inflated with 50 ml of air and the pressure was allowed to equilibrate for 3 minutes. The average bag pressure during the last 15 seconds defined the individual operating pressure (IOP) [17, 24], which is the minimum pressure required to overcome mechanical forces and inflate the bag with 50 ml of air. Next, pain thresholds were assessed using the ascending method of limits (AML) [24]. Phasic distentions were 30-seconds in duration and were separated by 30 second rest intervals starting at the IOP and progressively increasing in 2 mmHg steps until either the subject requested the research nurse to stop the protocol or 48 mmHg was reached. The pain threshold was defined as the amount of pressure above IOP at which the subject first reported moderate pain (absolute distending pressure *minus* the IOP). If the subject reached 48 mmHg without reporting moderate pain, the pain threshold was defined as 50 mmHg *minus* the IOP. The urge threshold was defined analogously. After measuring sensory thresholds, there was a 15 min rest period.

Phasic contractions were measured from the perfusion ports above and below the bag under the following conditions: (a) during the fasting baseline for 10 min at the IOP, (b) during distention for 10 min at a pressure of IOP+20 mmHg, (c) during a recovery period after intraluminal distention for 15 min at the IOP, and (d) following the meal for 30 min at the IOP. These tracings were visually screened to exclude artifact, defined as wave amplitudes

less than 5 mmHg or with durations less than 6 sec. The beginning and ending inflection points for each individual contraction were identified visually and the area under the curve was calculated using computer software (Insight System, Sandhill Scientific, Highlands Ranch, CO). These areas were added together, then divided by recording time in seconds (excluding the time occupied by movement artifact), and multiplied by 100. Separate motility indices (MI) were calculated for the two perfusion ports above the balloon and the two ports below the balloon.

Average barostat bag volumes in each period were recorded as a measure of smooth muscle tone [24]. Muscle tone was measured during the fasting baseline, recovery period after intraluminal distention, and following the meal. The average volume required to maintain the barostat bag at a constant pressure was recorded in successive 5 minute blocks; this constitutes an index of smooth muscle tone.

The test meal was standardized and contained 810 kcals and 38 grams of fat. Subjects were asked to consume the meal within 10 minutes. Phasic and tonic motility were recorded for a 30-minute period following the test meal (Figure 1). Details of all test procedures and descriptions of the questionnaires are given in the 2008 publication [17].

Data Analysis

Because the data were not normally distributed, comparisons between groups were made using the Kruskal-Wallis test, followed by Mann-Whitney U test for paired comparisons. A Bonferroni correction was also applied to correct for multiple comparisons. For all analyses, a p-value of 0.05 defined statistical significance. Although this is a large enough study to be reported comparing between patients with and without PI-IBS on physiological findings, the available samples were unequal in size (N=22 for PI-IBS, N=181 for NI-IBS and N=43 for controls), and consequently the statistical power of between group comparisons varied. To compensate for this limitation, we identified the minimum Z-score for a Mann-Whitney U test involving the smallest group (PI-IBS) that was significant at $P < 0.05$ and interpreted other comparisons as statistically significant only if they exceeded the critical value.

RESULTS

Characteristics of the eligible samples are shown in Table 1. Among the 218 IBS patients, 22 (10.1%) met criteria for PI-IBS. There were no differences among HC, PI-IBS, and NI-IBS for female ratio, age, or race/ethnicity. Twenty PI-IBS, 181 NI-IBS, and 34 HC underwent the colonic motility tests. No obvious mucosal abnormality or inflammation was confirmed in these subjects by colonoscopy. No serious adverse events were observed.

There was no significant difference in the proportion who were females or in the proportion with subtypes of bowel habit between PI-IBS and NI-IBS (Table 1). Both PI-IBS and NI-IBS patients scored significantly higher on the overall score and all subscales of the IBS-SSS and significantly lower on the IBS-QOL compared to HC (Table 1). Both PI-IBS and NI-IBS also scored significantly higher than HC on the BSI-18 global severity index for psychological distress and the somatization, depression and anxiety subscales. However,

there were no significant differences between patients with PI-IBS and NI-IBS on these variables (Table 1).

Pain Sensitivity and Urgency to Defecate

Both the PI-IBS and NI-IBS had significantly lower thresholds for pain and urgency to defecate compared to HC. Compared to NI-IBS, the PI-IBS failed to show significantly lower thresholds for pain or urge (Table 2).

Smooth Muscle Tone Measured by Barostat Bag Volume

PI-IBS patients showed significantly lower bag volumes than HC at baseline (Table 2 and Figure 2). There was no significant difference in bag volume during the baseline period between PI-IBS and NI-IBS. Muscle tone was not measured during distention because barostat bag volumes during distention reflect compliance rather than tone. Barostat bag volumes during recovery from distention were approximately the same as during baseline and showed no significant difference between PI-IBS and NI-IBS (Table 2). As shown in Figure 2, both HC and IBS groups showed a statistically significant and profound decrease in bag volumes following the meal. The magnitude of this change in muscle tone was not significantly different among PI-IBS, NI-IBS and HC.

Phasic Colonic Motility

When tested under baseline conditions (fasting, no intraluminal distention), the motility index for phasic contractions was no different among HC, NI-IBS and PI-IBS patients (Table 2).

As shown in Figure 3A, both IBS and HC groups showed a significant increase from baseline in motility index recorded from perfusion ports above the balloon during intraluminal distention. The magnitude of this increase was significantly greater in PI-IBS compared with NI-IBS ($p<0.05$) and HC ($p<0.01$). The colonic phasic motility response to distention in NI-IBS was significantly greater than that in HC ($p<0.05$). The increase in motility index from baseline to distention was significantly greater in PI-IBS (504% (110 to 1117%), median with inter quartile range) compared with NI-IBS (144% (21 to 483%), $p<0.05$) and HC (40% (−16 to 301%), $p<0.01$). Both IBS and HC groups showed a significant increase from baseline in motility index during intraluminal distention at the distal site (Figure 3B and Table 2). However, the magnitude of this increase was not significantly different among PI-IBS, NI-IBS and HC groups.

During the recovery period following intraluminal distention at the proximal site of the balloon, the motility index in PI-IBS was greater compared to NI-IBS and HC but the difference was not statistically significant (Figure 3A). The motility index at the distal site in PI-IBS was not significantly greater compared to HC or NI-IBS during the recovery period (Figure 3B).

As shown in Figure 3A and 3B, both HC and IBS groups showed significant increases in motility following the meal compared to baseline. The postprandial motility index recorded from perfusion ports below the balloon but not above the balloon, was significantly greater

in NI-IBS compared to HC ($p<0.05$, Figure 3B). However, the meal-stimulated increase in phasic contractions at the distal site in PI-IBS (174% (−1 to 317%)) was not significantly greater compared to NI-IBS (87% (18 to 376%)) or HC (87% (14 to 226%)).

DISCUSSION

This is the first study to compare physiological findings on colonic motility and visceral sensitivity between patients with a preceding infectious episode before the onset of IBS (PI-IBS) compared to those without an infectious episode (NI-IBS). This large, carefully conducted study yielded important and novel findings: Patients with PI-IBS showed more phasic contractions of the colon during intraluminal distention compared to NI-IBS and healthy controls, a significant increase in smooth muscle tone compared to HC at baseline, and a tendency for muscle tone to be higher in PI-IBS than in NI-IBS at baseline. However, there was no difference in IBS symptom severity, psychological symptoms, or visceral sensitivity to colonic distention between patients with PI-IBS and those with NI-IBS (Table 1). Prevalence of PI-IBS in the unselected patients with IBS in the present study is similar with the previous reports from epidemiological studies [25]. In addition, the proportion of subtypes of bowel habit in our patients with PI-IBS was in accordance with the previous findings from a long-term cohort study [26].

Colonic Motility Responses in PI-IBS

The pathophysiological mechanisms involved in PI-IBS are currently unknown. We have previously reported that IBS patients show hypercontractility during colonic distention independent of their bowel habit subtype [17]. It has been reported that rectal hypersensitivity and accelerated whole gut transit were exhibited in both patients with PI-IBS and patients who returned to normal bowel habit following an infectious episode [13]. However, differences in gut motor and sensory function has not been evaluated between PI-IBS and NI-IBS until now.

Our findings are consistent with animal studies showing that transient enteric infection can lead to persistent gut dysmotility in nematode-infected mice [11]. Animal studies have demonstrated that inflammation-induced intestinal muscle hypercontractility persists even after resolution of the inflammation [12, 27] and that increases in muscle contractility are associated with increases in intestinal 5-HT and infiltration of immunocytes [28]. Several reports on histologic and immunohistochemical analyses in the intestinal mucosa [7, 14, 29] suggest that subtle morphologic changes involving lymphocytes, mast cells, enterochromaffin (EC) cells which contain serotonin, and enteric nerves may be associated with IBS symptoms. This low-grade intestinal mucosal inflammation along with mast cell hyperplasia might contribute to the development and perpetuation of abnormal motility patterns and visceral hypersensitivity in IBS by increasing mucosal 5-HT release and availability. Gut inflammation increases the number of EC cells, which is mediated by T lymphocytes [30], as has been reported in PI-IBS [19], and inflammation reduces SERT [31]. In addition, 5-HT spontaneous secretion is correlated with mast cell counts and the severity of abdominal pain in patients with IBS [32]. Interestingly, the 5-HT3 antagonist alosetron actually decreased rectal tone in patients with diarrhea-predominant IBS [33].

Colonic Visceral Sensitivity and Psychological Factors in PI-IBS

Even mild acute colitis can induce long-lasting visceral hyperalgesia in a rat model [34]. Moreover, intestinal effluents from IBS patients activate visceral sensory afferent pathways when applied to the mucosa of an animal model, and this effect is mediated by proteases released by activated mast cells [35]. There is also a positive correlation between the number of activated mast cells in close proximity to nerve endings and the severity of abdominal pain in IBS patients [36]. Consequently, in the present study PI-IBS patients were expected to have a lower pain threshold than NI-IBS, but the groups were not found to be significantly different. This lack of effect could be due to low statistical power.

Cognitive and psychological factors also influence pain reporting: We have shown that pain threshold in patients with IBS are significantly correlated with somatization and anxiety [37], and brain imaging studies reveal that visceral stimuli activate affective and/or cognitive regions such as the dorsal anterior cingulate cortex (dACC) in patients with IBS [38, 39]. These centrally mediated processes may play an important role in the pathophysiology of visceral sensitivity in IBS, and this effect may be independent of gastroenteritis. This would be consistent with the findings of this study which showed significant elevations for both groups of IBS patients on all subscales of the BSI-18 but no differences in pain or urge thresholds between PI-IBS and NI-IBS.

Study Limitations

The small number of PI-IBS cases identified in this study resulted in modest statistical power; with a larger sample of PI-IBS patients the trend towards a difference in baseline muscle tone between PI-IBS and NI-IBS might be found to be statistically significant. In the present study, only a 10-min baseline period for the motility measurement was set to avoid a prolonged experimental time. Therefore, the motility recordings were carefully performed by observing the baseline stabilization after a sufficient rest (over 30 minutes).

A second limitation was that the diagnosis of PI-IBS was based on retrospective reports of an episode of gastroenteritis preceding the onset of IBS symptoms and the absence of IBS preceding this episode of gastroenteritis. We do not think this was a major source of case misclassification because the rate of PI-IBS (10.1% of IBS patients) was similar to what has been reported in the literature (6% to 17%) [25]. Moreover, we used published criteria for inferring the presence of PI-IBS [19] although detailed features of the acute infectious episode (e.g. duration of diarrhea, weight loss, and bloody stool) which may be associated with the risk factors of PI-IBS [10] were not evaluated. It is noted that no difference was found in characteristics of IBS samples for the analyses between patients already reported elsewhere [17] and the additional patients including age, female ratio, race/ethnicity, IBS symptom severity or prevalence of PI-IBS in the present study (data were not shown).

A third limitation is that a variable amount of time – often several years – elapsed between the episode of infectious gastroenteritis and the subject's participation in this study, and some potential moderators of the risk of developing PI-IBS such as re-exposure to gastrointestinal pathogens and changes in psychological symptoms of anxiety and depression may have occurred during this interval. This would reduce the chances of

identifying a significant association between these variables and the occurrence of PI-IBS. However, when a significant difference between PI-IBS and NI-IBS such as the difference in phasic motility response to distention is observed years after the enteric infection, this can be interpreted as evidence that the past enteric infection was the cause.

The present study would have been enhanced if we had collected mucosal biopsies or stool specimens and tested for increased numbers of EC cells, immune cells such as mast cells, or inflammatory mediators in the gut mucosa. It has been reported that a greater number of EC cells is associated with visceral hypersensitivity in patients with IBS [40]. Experimental studies in animals support the findings that PI-IBS shows colonic hypercontractility during noxious stimulation of the gut [12, 27], and our study confirms this in human IBS patients. Further prospective observations of the relationships between such a physiological exacerbation and changes in mucosal immunocyte infiltration [13, 14], epithelial permeability [15] and composition of gut microbiome [41, 42] are needed to confirm the hypothesis that the exaggerated motility responses to distention are mediated by persisting immune activation.

Conclusions

PI-IBS is considered to be a good model for investigating the etiology and pathophysiology of IBS because PI-IBS identifies a more homogeneous subset of patients. This study shows that approximately 10% of IBS patients have an infectious etiology and that the principal physiological difference between PI-IBS and NI-IBS is greater colonic hypercontractility during intraluminal distention. This pattern of hypercontractility was not limited to one bowel habit subtype of IBS, although others have found diarrhea to be more common than constipation in PI-IBS. There were no significant differences between PI-IBS and NI-IBS in IBS symptom severity, psychological symptoms, resting smooth muscle tone or visceral pain sensitivity even though IBS patients in general (both PI-IBS and NI-IBS) were significantly different from healthy controls in these regards. This suggests that the physiological mechanisms for symptoms are generally similar for PI-IBS and NI-IBS and that PI-IBS is a part of IBS rather than being a distinctly different disorder. It remains to be investigated whether PI-IBS patients will respond to different treatments than other types of IBS. The most likely candidate for a PI-IBS-specific treatment is a motility agent or a mast cell stabilizer.

Acknowledgments

This study was supported by grants R01 DK31369, R24 DK67674, and M01 RR00046.

Abbreviations

IBS	irritable bowel syndrome
PI-IBS	post-infectious irritable bowel syndrome
NI-IBS	non-post-infectious irritable bowel syndrome
IBS-SS	Irritable Bowel Syndrome Severity Scale

BSI	Brief Symptom Inventory
AML	ascending method of limits
IOP	individual operating pressure

References

1. Drossman DA, Camilleri M, Mayer EA, Whitehead WE. AGA technical review on irritable bowel syndrome. Gastroenterology. 2002; 123:2108–31. [PubMed: 12454866]
2. Drossman DA, Creed FH, Olden KW, Svedlund J, Toner BB, Whitehead WE. Psychosocial aspects of the functional gastrointestinal disorders. Gut. 1999; 45(Suppl 2):II25–30. [PubMed: 10457041]
3. Spiller R, Garsed K. Postinfectious irritable bowel syndrome. Gastroenterology. 2009; 136:1979–88. [PubMed: 19457422]
4. Chaudhary N, Truelove S. The irritable colon syndrome. A study of the clinical features, predisposing causes, and prognosis in 130 cases. Q J Med. 1962; 31:307–22. [PubMed: 13878459]
5. Gwee KA, Graham JC, McKendrick MW, et al. Psychometric scores and persistence of irritable bowel after infectious diarrhoea. Lancet. 1996; 347:150–3. [PubMed: 8544549]
6. Neal KR, Barker L, Spiller RC. Prognosis in post-infective irritable bowel syndrome: a six year follow up study. Gut. 2002; 51:410–3. [PubMed: 12171965]
7. Dunlop SP, Jenkins D, Neal KR, Spiller RC. Relative importance of enterochromaffin cell hyperplasia, anxiety, and depression in postinfectious IBS. Gastroenterology. 2003; 125:1651–9. [PubMed: 14724817]
8. Mearin F, Perez-Oliveras M, Perello A, et al. Dyspepsia and irritable bowel syndrome after a Salmonella gastroenteritis outbreak: one-year follow-up cohort study. Gastroenterology. 2005; 129:98–104. [PubMed: 16012939]
9. Marshall JK, Thabane M, Garg AX, Clark WF, Salvadori M, Collins SM. Incidence and epidemiology of irritable bowel syndrome after a large waterborne outbreak of bacterial dysentery. Gastroenterology. 2006; 131:445–50. [PubMed: 16890598]
10. Thabane M, Simunovic M, Akhtar-Danesh N, et al. Development and validation of a risk score for post-infectious irritable bowel syndrome. Am J Gastroenterol. 2009; 104:2267–74. [PubMed: 19568228]
11. Bercik P, Wang L, Verdu EF, et al. Visceral hyperalgeria and intestinal dysmotility in a mouse model of postinfective bowel dysfunction. Gastroenterology. 2004; 127:179–87. [PubMed: 15236184]
12. Barbara G, Vallance BA, Collins SM. Persistent intestinal neuromuscular dysfunction after acute nematode infection in mice. Gastroenterology. 1997; 113:1224–32. [PubMed: 9322517]
13. Gwee KA, Leong YL, Graham C, et al. The role of psychological and biological factors in postinfective gut dysfunction. Gut. 1999; 44:400–6. [PubMed: 10026328]
14. Spiller RC, Jenkins D, Thornley JP, et al. Increased rectal mucosal enteroendocrine cells, T lymphocytes, and increased gut permeability following acute campylobacter enteritis and in post-dysenteric irritable bowel syndrome. Gut. 2000; 47:804–11. [PubMed: 11076879]
15. Dunlop SP, Hebden J, Campbell E, et al. Abnormal intestinal permeability in subgroups of diarrhea-predominant irritable bowel syndromes. Am J Gastroenterol. 2006; 101:1288–94. [PubMed: 16771951]
16. Bergin AJ, Donnelly TC, McKendrick MW, Read NW. Changes in anorectal function in persistent bowel disturbance following salmonella gastroenteritis. Eur J Gastroenterol Hepatol. 1993; 5:617–20.
17. Kanazawa M, Palsson OS, Thiwan SIM, et al. Contributions of pain sensitivity and colonic motility to IBS symptom severity and predominant bowel habits. Am J Gastroenterol. 2008; 103:2550–61. [PubMed: 18684175]

18. Longstreth, GF.; Thompson, WG.; Chey, WD.; Houghton, LA.; Mearin, F.; Spiller, RC. Functional bowel disorders. In: Drossman, DA.; Corazziari, E.; Delvaux, M., et al., editors. Rome III: The functional gastrointestinal disorders. 3rd. McLean, VA: Degnon Associates; 2006. p. 487-555.
19. Dunlop SP, Jenkins D, Spiller RC. Distinctive clinical, psychological, and histological features of postinfective irritable bowel syndrome. Am J Gastroenterol. 2003; 98:1578–83. [PubMed: 12873581]
20. Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: A simple method of monitoring irritable bowel syndrome and its progress. Aliment Pharmacol Ther. 1997; 11:395–402. [PubMed: 9146781]
21. Patrick DL, Drossman DA, Frederick IO, DiCesare J, Puder KL. Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. Dig Dis Sci. 1998; 43:400–11. [PubMed: 9512138]
22. Drossman DA, Patrick DL, Whitehead WE, et al. Further validation of the IBS-QOL: a disease-specific quality-of-life questionnaire. Am J Gastroenterol. 2000; 95:999–1007. [PubMed: 10763950]
23. Derogatis, LR. BSI 18 Brief Symptom Inventory 18: Administration, scoring, and procedures manual. NCS Pearson Inc; 2000.
24. Whitehead WE, Delvaux M, Azpiroz F. Standardization of barostat procedures for testing smooth muscle tone and sensory thresholds in the gastrointestinal tract. Dig Dis Sci. 1997; 42:223–41. [PubMed: 9052500]
25. Longstreth GF, Hawkey CJ, Mayer EA, et al. Characteristics of patients with irritable bowel syndrome recruited from three sources: implications for clinical trials. Aliment Pharmacol Ther. 2001; 15:959–64. [PubMed: 11421870]
26. Marshall JK, Thabane M, Garg AX, et al. Walkerton Health Study Investigators. Eight year prognosis of postinfectious irritable bowel syndrome following waterborne bacterial dysentery. Gut. 2010; 59:605–11. [PubMed: 20427395]
27. Akiho H, Deng Y, Blennerhassett P, Kanbayashi H, Collins SM. Mechanisms underlying the maintenance of muscle hypercontractility in a model of postinfective gut dysfunction. Gastroenterology. 2005; 129:131–41. [PubMed: 16012943]
28. Mizutani T, Akiho H, Khan WI, et al. Persistent gut motor dysfunction in a murine model of T-cell-induced enteropathy. Neurogastroenterol Motil. 2010; 22:196–203. [PubMed: 19735478]
29. Buhner S, Li Q, Vignali S, et al. Activation of human enteric neurons by supernatants of colonic biopsy specimens from patients with irritable bowel syndrome. Gastroenterology. 2009; 137:1425–34. [PubMed: 19596012]
30. Motomura Y, Ghia JE, Wang H, et al. Enterochromaffin cell and 5-hydroxytryptamine responses to the same infectious agent differ in Th1 and Th2 dominant environments. Gut. 2008; 57:475–81. [PubMed: 18198200]
31. Foley S, Garsed K, Singh G, et al. Impaired uptake of serotonin by platelets from patients with irritable bowel syndrome correlates with duodenal immune activation. Gastroenterology. 2011; 140:1434–43. [PubMed: 21315720]
32. Cremon C, Carini G, Wang B, et al. Intestinal serotonin release, sensory neuron activation, and abdominal pain in irritable bowel syndrome. Am J Gastroenterol. 2011; 106:1290–8. [PubMed: 21427712]
33. Delvaux M, Louvel D, Mamet JP, et al. Effect of alosetron on responses to colonic distension in patients with irritable bowel syndrome. Aliment Pharmacol Ther. 1998; 12:849–55. [PubMed: 9768527]
34. Adam B, Liebregts T, Gschossmann JM, et al. Severity of mucosal inflammation as a predictor for alterations of visceral sensory function in a rat model. Pain. 2006; 123:179–86. [PubMed: 16630696]
35. Barbara G, Wang B, Stanghellini V, et al. Mast cell-dependent excitation of visceral-nociceptive sensory neurons in irritable bowel syndrome. Gastroenterology. 2007; 132:26–37. [PubMed: 17241857]

36. Barbara G, Stanghellini V, De Giorgio R, et al. Activated mast cells in proximity to colonic nerves correlate with abdominal pain in irritable bowel syndrome. Gastroenterology. 2004; 126:693–702. [PubMed: 14988823]

37. Dorn SD, Palsson OS, Thiwan SIM, et al. Colonic pain sensitivity in irritable bowel syndrome is the result of an increased tendency to report pain rather than increased neurosensory sensitivity. Gut. 2007; 56:1202–9. [PubMed: 17483191]

38. Mertz H, Morgan V, Tanner G, et al. Regional cerebral activation in irritable bowel syndrome and control subjects with painful and nonpainful rectal distention. Gastroenterology. 2000; 118:842–8. [PubMed: 10784583]

39. Mayer EA, Berman S, Suyenobu B, et al. Differences in brain responses to visceral pain between patients with irritable bowel syndrome and ulcerative colitis. Pain. 2005; 115:398–409. [PubMed: 15911167]

40. Park JH, Rhee PL, Kim HS, et al. Mucosal mast cell counts correlate with visceral hypersensitivity in patients with diarrhea predominant irritable bowel syndrome. J Gastroenterol Hepatol. 2006; 21:71–8. [PubMed: 16706815]

41. Posserud I, Stotzer PO, Björnsson ES, Abrahamsson H, Simrén M. Small intestinal bacterial overgrowth in patients with irritable bowel syndrome. Gut. 2007; 56:802–8. [PubMed: 17148502]

42. Grover M, Kanazawa M, Palsson OS, et al. Small intestinal bacterial overgrowth in irritable bowel syndrome: association with colon motility, bowel symptoms, and psychological distress. Neurogastroenterol Motil. 2008; 20:998–1008. [PubMed: 18482250]

Key Messages

The aim of the study was to investigate whether post-infectious IBS (PI-IBS) is associated with colonic motility and sensory abnormalities compared to non-PI-IBS (NI-IBS) or healthy controls (HC).

Colonic motility and visceral pain threshold to intraluminal distentions were compared using manometric and barostat devices.

PI-IBS patients demonstrated increased colonic contractility during distention compared to NI-IBS and HC. PI-IBS and NI-IBS patients were similar in pain threshold, IBS symptom severity, IBS-Quality of Life impact, and psychological symptoms suggesting that PI-IBS is not a distinct subtype of IBS.

Modulation of gut irritation and motility agents should be taken into account for management of IBS.

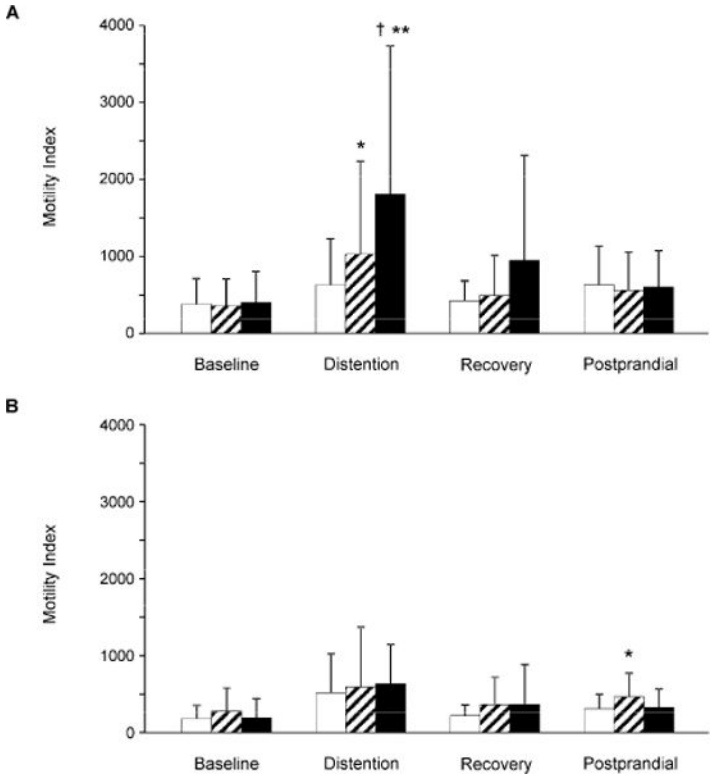

Figure 1.

The sequence of events during the study. AML, ascending method of limits; IOP, individual operating pressure.

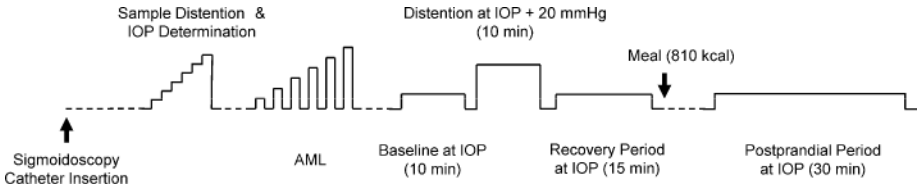

Figure 2.

Colonic tonic motility responses. Mean barostat bag volumes with standard deviation were shown during baseline, recovery and postprandial periods. Muscle tone was not measured during distention because barostat bag volumes during distention reflect compliance rather than tone. Open bars, healthy controls (HC); hatched bars, non-post-infectious-IBS (NI-IBS); closed bars, post-infectious IBS (PI-IBS). *$p<0.05$ vs. HC.

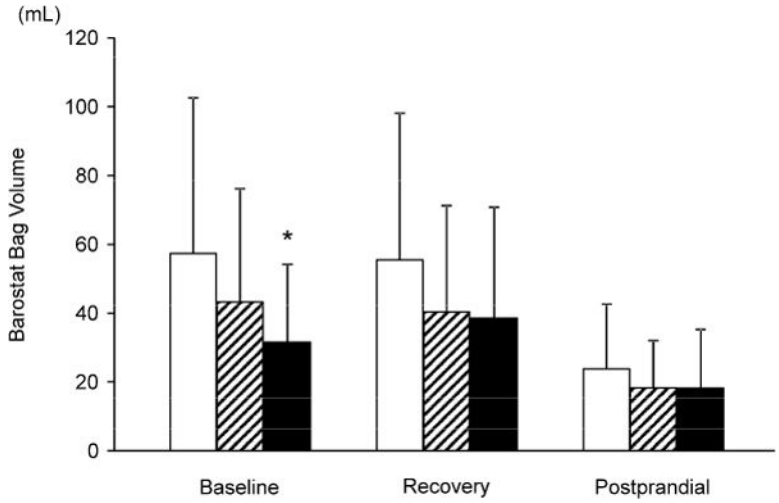

Figure 3.

Colonic phasic motility responses. Mean motility indices recorded from perfusion ports above the balloon (**A**) and bellow the balloon (**B**) placed into the descending colon with standard deviation were shown during the baseline (at IOP), distention (at IOP+20 mmHg), recovery (at IOP) and postprandial periods (at IOP). Open bars, healthy controls (HC); hatched bars, non-post-infectious-IBS (NI-IBS); closed bars, post-infectious IBS (PI-IBS). *p<0.05, **p<0.01 vs. HC; †p<0.05 vs. NI-IBS.

Table 1

Characteristics of the participants

	HC	NI-IBS	PI-IBS
Number (female%)	43 (81%)	196 (83%)	22 (82%)
Age (yrs)	38 ± 13	33 ± 11	36 ± 11
Subtypes of bowel habit			
Diarrhea	–	65 (33%)	10 (46%)
Mixed	–	85 (43%)	8 (36%)
Constipation	–	32 (16%)	3 (14%)
Unspecified	–	14 (7%)	1 (4%)
IBS-SSS (overall)	29 ± 52	276 ± 90**	261 ± 94**
Pain intensity	3 ± 11	46 ± 25**	49 ± 26**
Pain duration	5 ± 12	47 ± 23**	48 ± 26**
Abdominal bloating	3 ± 8	47 ± 29**	36 ± 32**
Dissatisfaction of bowel habit	17 ± 29	77 ± 23**	73 ± 26**
Disturbed daily activity	4 ± 14	59 ± 28**	55 ± 31**
IBS-QOL	99 ± 3	69 ± 21**	70 ± 20**
BSI-18 general severity index	42 ± 8	51 ± 10**	53 ± 10**
Somatization	45 ± 6	53 ± 8**	54 ± 9**
Depression	46 ± 8	51 ± 11**	52 ± 12*
Anxiety	43 ± 6	50 ± 9**	50 ± 11**

Data were expressed as mean ± SD.

* $p<0.05$

** $p<0.01$, vs. HC.

Table 2

Sensory thresholds and colonic motility responses.

	HC	NI-IBS	PI-IBS
Pain threshold (mmHg)	40 (30–42)	30 (20–38)**	32 (13–42)**
Urge threshold (mmHg)	34 (22–42)	17 (11–30)**	17 (9–38)**
IOP (mmHg)	8 (6–10)	10 (8–12)	8 (7–10)
Barostat bag volume (mL)			
Baseline at IOP	50 (20–84)	36 (18–56)	36 (15–56)*
Recovery at IOP	42 (20–80)	32 (17–59)	40 (14–89)
Postprandial period at IOP	17 (11–27)	15 (12–20)	14 (10–20)
Motility index above the balloon			
Baseline	310 (196–546)	263 (143–677)	499 (129–792)
Distention	407 (300–758)	800 (448–1308)*	1011 (562–3357)**,†
Recovery	369 (206–526)	345 (151–804)	633 (345–1267)
Postprandial period	543 (295–901)	446 (223–835)	510 (235–685)
Motility index below the balloon			
Baseline	141 (74–274)	187 (107–397)	122 (71–535)
Distention	462 (234–614)	345 (180–703)	508 (118–758)
Recovery	186 (71–325)	310 (121–426)	204 (127–251)
Postprandial period	286 (139–418)	434 (202–628)*	239 (118–381)

IOP, individual operating pressure. Data were expressed as median with inter quartile range.

* $p<0.05$

** $p<0.01$ vs. HC;

† $p<0.05$ vs. NI-IBS.