Journal of Pediatric Gastroenterology and Nutrition
46:272–278 © 2008 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

Is Visceral Hypersensitivity Correlated With Symptom Severity in Children With Functional Gastrointestinal Disorders?

Julie Castilloux, Angela Noble, and Christophe Faure

Department of Pediatrics, Division of Pediatric Gastroenterology, Hôpital Sainte-Justine, Université de Montréal, Montréal, Quebec, Canada

ABSTRACT

Background: Abdominal pain related to irritable bowel syndrome (IBS) and functional abdominal pain (FAP) is frequent in children and can be of variable severity. Both IBS and FAP are associated with rectal hypersensitivity. We hypothesized that in children with IBS and FAP, the rectal sensory threshold for pain (RSTP) is associated with symptom severity.

Paitents and Methods: A total of 47 patients (34 girls; median age, 14.2 years) with IBS (n = 29) and FAP (n = 18), according to the Rome II criteria, underwent a rectal barostat examination to determine their RSTP. Gastrointestinal symptom severity was assessed by validated questionnaires. During the rectal barostat exam, symptoms were documented using a visual analog scale and by measuring the area coloured on a human body diagram corresponding to painful sensations.

Results: The median RSTP was 16 mmHg and was similar in IBS and FAP patients. Eighty-three percent of the patients had rectal hypersensitivity (RSTP $\leq$ 30.8 mmHg, the 5th percentile of control children studied in our laboratory). Fifty-one percent and 36%, respectively, reported missing school and social activities at least once per week. Increased frequency of pain, missed days of school, missed social activities, and pain during the barostat examination were not associated with lower RSTP values in either the whole group or in the subset of children with rectal hypersensitivity.

Conclusions: Rectal hypersensitivity is not proportional to the severity of symptoms in children with IBS and FAP, indicating that symptom severity is influenced by other factors in addition to visceral hypersensitivity. ***JPGN 46:272–278, 2008.*** **Key Words:** Children—Functional abdominal pain—Irritable bowel syndrome—Rectal barostat—Rome II criteria—Visceral sensitivity. © 2008 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

Recurrent abdominal pain in children is a common indication for consultation to pediatric gastroenterology outpatient clinics. Functional gastrointestinal disorders (FGID) represent the vast majority of these cases (1–3) and are of variable severity. Not uncommonly, they have a significant impact on a child's quality of life secondary to increased frequency of doctor visits and the interruption of normal school and social activities (4–6).

In the last few years, studies have shown that functional abdominal pain (FAP) and irritable bowel syndrome (IBS) are highly associated with rectal hypersensitivity in adults and children (7–12). In adults, the pathophysiology of abdominal pain in FGID involves complex mechanisms associated with visceral hypersensitivity, in addition to other factors such as anomalies of pain perception, anxiety, depression, and somatization (13,14).

Received May 3, 2007; accepted July 3, 2007.

Address correspondence and reprint requests to Christophe Faure, MD, Division of Gastroenterology and Nutrition, Hôpital Ste-Justine, 3175 Côte Ste Catherine, Montréal, Québec, Canada, H3T 1C5 (e-mail: christophe.faure@umontreal.ca).

The authors report no conflicts of interest.

In children, mechanisms involved in FGID also are complex and similarly have been associated with visceral hypersensitivity and psychosocial factors (15–17). However, no data are available regarding the relation between symptom severity reported by children with FGID and their level of visceral hypersensitivity.

The present study was designed to test the hypothesis that in children with abdominal pain related to IBS or FAP, the rectal sensory threshold of pain (RSTP) is associated with symptom severity. The objectives were to measure the RSTP in IBS and FAP children, evaluate the symptom severity in this population, and determine the association between RSTP- and FGID-related symptom severity.

PATIENTS AND METHODS

Children referred for chronic abdominal pain to the tertiary care pediatric gastroenterology outpatient clinic at the Hôpital Sainte-Justine were evaluated by experienced pediatric gastroenterologists. Children ages 8 to 18 years subsequently diagnosed with either IBS or FAP, as per the pediatric Rome II criteria, were recruited for this study. Children with a history of

rectocolonic surgery, encopresis, fecal impaction, neurological issues, or muscular problems were excluded. Children unable to collaborate with the study protocol also were excluded. All of the medications affecting pain or gastrointestinal motility were discontinued at least 48 hours before the barostat procedure. The ethics and research committee at the Hôpital Sainte-Justine approved the study protocol. Parents and children gave informed consent and assent, respectively, before participating in the study. The barostat exam results of 29 of the children included in this study were reported in a previous article (12).

Questionnaires

The participants completed the Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS), State-Trait Anxiety Inventory for Children (STAIC), and Child Depression Inventory (CDI). The QPGS is a questionnaire that was developed and validated in English and French at the Hôpital Sainte-Justine (2,18,19). It assesses symptoms associated with FGID in children, as specified by the pediatric Rome II criteria (20). This structured questionnaire includes sections assessing children's bowel habits, abdominal pain (pain duration and frequency), and limitations in activities (missed days of school and missed activities with friends because of pain). The STAIC is a 20-item questionnaire validated in children that assesses symptoms of anxiety. STAIC scores >68 have been shown to reflect a state and/or trait of anxiety (21). The CDI is a 27-item questionnaire that has been validated in children for the evaluation of depression; CDI scores >17 correlate with clinical depression (22). French translations of both the STAIC and CDI questionnaires have been validated in French-Canadian children (21,22). All of the questionnaires were completed before the barostat procedure by the child or with the help of a parent if the child was <10 years old.

Barostat Procedure

RSTP was measured with an electronic barostat (G & J Electronics, Toronto), as previously described (12) and according to published recommendations (23). After a 6-hour fasting period, a double-canal catheter of 18F diameter—on which a spherical polyvinyl bag (Mui Scientific, Mississauga, Canada) was fixed—was inserted into the rectum. The catheter was then secured with tape and 5 to 10 minutes were allowed for adaptation before beginning the procedure. The length of the inflated bag was 11 cm, and its maximal theoretical capacity was 600 mL. Its compliance is considered infinite. The bag was checked for leaks at the beginning and at the end of each experiment. The barostat was programmed to deliver phasic intermittent stimuli lasting 60 seconds followed by 60 seconds of deflation according to the ascending method of limits with tracking. A 4-point scale was used as a verbal descriptor for sensation felt during the barostat procedure. The rectal sensory threshold was determined by averaging the pressures at which pain had been indicated. The maximal pressure was 48 mmHg. When a painful sensation was felt, a visual analog scale (VAS) was used to quantify the intensity of the pain. The pain also was specified with the following measurement method: the children were instructed to indicate on a standardized human body diagram (seen from front and back) (12,24) any painful sensation experienced during the procedure. The figures were scanned and processed for the measurement of areas of coloured zones with National Institutes of Health ImageJ software (*http://rsb.info.nih.gov/ij*) (12,24). The area of the coloured zones is presented in pixels.

Rectal compliance was calculated using a nonlinear model for fitting the pressure-volume curves of each individual. The pressure-volume curves were constructed using the average calculated volume during the 60 seconds of each consecutive pressure step. The compliance was calculated as the maximum slope in the pressure-volume curve (23,25). The RSTP and the compliance findings in our study population were compared with normal values established in 10 control children (median age, 13.7 years; range, 10.2–16.1 years) studied under the same conditions in our laboratory (12).

Assessment of Symptom Severity

The evaluation of abdominal pain in children requires a multidimensional measure (6). Given this, the severity and impact of the gastrointestinal symptoms were assessed by the QPGS (duration and frequency of pain, impact on daily life), the evaluation of abdominal pain induced during the barostat procedure (VAS and the area that was coloured), and the STAIC and CDI questionnaires. The assessment of anxiety and depression was included, given that both have been shown to be important cofactors in FGID, contributing to lower quality of life scores in affected children (4).

Statistics

Descriptive statistics were used to summarize the demographic characteristics of the population, questionnaire findings, and barostat examination results. Summary data is expressed as means ($\pm$ standard deviation) for normally distributed data and medians (25th–75th percentile, or interquartile range [IQR]) for non–normally distributed data. Comparisons between the IBS and FAP groups used the Student t test to compare means for the normally distributed continuous variables, the Mann-Whitney U test for non–normally distributed variables, and the chi-square or Fisher exact test for count data.

Univariate logistic and linear regression was used to determine the association between normal versus abnormal RSTP and the symptom severity variables (frequency of reported pain, duration of symptoms, missed days at school, missed activities with friends, VAS, and area coloured on the human body diagram during the barostat procedure) and potential confounders (age, sex, and the presence of anxiety and clinical depression). The ordinal variables were dichotomized into clinically significant groups. A sensitivity analysis was done to ensure that alternate methods of dichotomizing these variables did not affect the analysis. Within the subgroup with abnormal RSTP results (RSTP $\leq$30.8 mmHg) (12), univariate logistic and linear regression was again used to test the association between decreases in RSTP level and the measures of symptom severity, anxiety, and depression. A $P < 0.05$ was considered of statistical significance. All of the analyses were performed with Stata 9.0 (Stata, Chicago, IL).

TABLE 1. *Demographics and rectal sensory threshold for pain (RSTP) of the study population*

	IBS (n = 29)	FAP (n = 18)	Both (n = 47)
Sex (male:female)	9:20	4:14	13:34
Age (years; median, IRQ)	15.4 (12.5–17)	13.3 (11.6–15.1)	14.2 (8.5–17.6)[†]
RSTP (mmHg; median, IRQ)	16 (12–26)	26 (12–28.5)	16 (2–48)[†]
No. of hypersensitive patients[*] (%)	23 (79)	16 (89)	39 (83)[†]

IBS = irritable bowel syndrome; FAP = functional abdominal pain; IRQ = interquartile range.
[*] RSTP ≤ 30.8 mmHg (12).
[†] Range.

RESULTS

Population and Barostat Results

Forty-seven children (34 girls) with a median age of 14.2 years (range, 8.5–17.6 years) were recruited for the study. Twenty-nine fulfilled the Rome II criteria for IBS and 18 for FAP as per the attending physician assessment and confirmed by the symptoms reported in the QPGS.

The median RSTP was 16 mmHg (IQR, 12–26 mmHg) in patients with IBS and 26 mmHg (IQR, 12–28.5) in patients with FAP. This was significantly lower than the RSTP values found in our previously reported control group (median, 40 mmHg; IQR, 32–48) ($P < 0.001$) (12). RSTP values were not statistically different in patients with IBS and FAP ($P = 0.52$) (Table 1). Eighty-three percent of the patients had rectal hypersensitivity as defined by an RSTP ≤30.8 mmHg; this represents the 5th percentile of the RSTP values measured in our control group, our cutoff score for rectal hypersensitivity (12). The rectal compliance was similar in the patients (7.7 mL/mmHg; IQR, 5.9–13.7) and in the controls (8.7 mL/mmHg; IQR, 6.0–10.1) ($P = 0.5$).

Symptom Severity

Symptom severity variables are provided in Table 2. There was no significant difference between the patients with IBS and FAP for symptom severity, or presence of anxiety or depression. Thirty-eight children (81%) reported abdominal pain for >1 year. Forty-six children (98%) had pain once per week or more and 24 (51%) and

TABLE 2. *Symptom severity variables in the study population*

	IBS (n = 29)	FAP (n = 18)	Both (n = 47)
Pain frequency, no. (%)			
≤ 1/wk	2 (7)	0 (0)	2 (4)
Many times per week	18 (62)	6 (33)	24 (51)
Daily	9 (31)	12 (67)	21 (45)
Duration of pain, no. (%)			
3 mo	1 (3)	0 (0)	1 (2)
4–11 mo	7 (24)	1 (6)	8 (17)
≥ 1 y	21 (72)	17 (94)	38 (81)
Missed days of school, no. (%)			
Never	7 (24)	5 (28)	12 (26)
<1/mo	6 (21)	0 (0)	6 (13)
1–4/mo	7 (24)	5 (28)	12 (26)
Many times per week	6 (21)	6 (33)	12 (26)
Daily	2 (7)	2 (11)	4 (9)
Missed activities with friends, no. (%)			
Never	3 (10)	4 (22)	7 (15)
<1/mo	8 (28)	3 (17)	11 (23)
1–4/mo	9 (38)	5 (28)	14 (30)
Many times per week	6 (21)	4 (22)	10 (21)
Daily	2 (7)	2 (11)	4 (9)
STAIC total score, mean (SD)	73 (9.3)	73 (11.1)	73 (9.8)
STAIC >68, no. (%)	15 (58)	9 (64)	24 (51)
CDI score (median, IQR)	8 (6–12)	9.5 (7–13)	9 (7–13)
CDI >17, no. (%)	3 (11)	1 (6)	4 (9)
Area coloured during barostat, median no. pixels (IQR)	18,099 (13,356–31,104)	16,408 (11,995–35,384)	17,889 (13,229–31,006)
VAS score, mean (SD)	4.8 (2.4)	5.4 (2.2)	5.0 (2.4)

IBS = irritable bowel syndrome; FAP = functional abdominal pain; STAIC = State-Trait Anxiety Inventory for Children; SD = standard deviation; CDI = Child Depression Inventory; IQR = interquartile range; VAS = visual analog scale.

17 (36%), respectively, reported missing school and social activities at least once per week.

Twenty-four patients (51%) had an anxiety problem (STAIC >68) and 4 patients (9%) had clinical depression (CDI >17). CDI and STAIC scores were significantly correlated ($r = 0.50$, $P = 0.01$). The presence of an anxiety problem was not associated with symptom severity (univariate logistic and linear regression; $P > 0.2$). The number of children with clinical depression (9%) did not allow meaningful testing of its association with symptom severity.

Relation Between Symptom Severity and RSTP

There was no significant difference between patients with IBS and FAP for age, sex, distribution of RSTP, rectal compliance, symptom severity, or presence of anxiety or depression (Tables 1 and 2); therefore, the groups were combined for all further analyses.

The distribution of the severity of symptom variables and potential confounding variables by rectal hypersensitivity is found in Table 3. Scatterplots and univariate logistic regression did not demonstrate an association between the severity of symptoms variables (frequency of pain, duration of symptoms, missed school and social activities, VAS and area coloured during the barostat examination) or abnormal STAIC scores (STAIC >68) and the presence of rectal hypersensitivity (RSTP values ≤30.8 mmHg) (Table 4). Age was not associated with RSTP values, severity of symptoms, or STAIC scores. Similarly, sex was not associated with severity of symptoms or STAIC scores, although a higher percentage of females had rectal hypersensitivity. The number of children with depression, as per the CDI, was too small to determine its association with RSTP, although all 4 of these children had rectal hypersensitivity.

Subsequent analysis with RSTP as a continuous variable similarly did not demonstrate any association between RSTP and symptom severity or anxiety. Sensitivity analysis with different cutoff points for the dichotomisation of the ordinal variables was negative.

Analysis of the subset of children with rectal hypersensitivity (RSTP ≤30.8 mmHg) demonstrated that lower RSTP values were not predictive of increased symptom severity (frequency of pain, missed days of school,

TABLE 3. *Distribution of symptom severity variables in patients with rectal hypersensitivity and in patients without rectal hypersensitivity*

	Patients with rectal hypersensitivity* (n = 39)	Patients without rectal hypersensitivity (n = 8)
Age, median (IQR)	14.2 (12.3–15.8)	14 (10–17)
Female sex (%)	31 (79)	3 (38)
Pain frequency, no. (%)		
≤1/wk	1 (2)	1 (12)
Many times per week	18 (46)	6 (75)
Daily	20 (51)	1 (12)
Duration of pain, no. (%)		
3 mo	1 (2)	0 (0)
4–11 mo	7 (18)	1 (12)
≥ 1 y	31 (80)	7 (88)
Missed days of school, no. (%)		
Never	9 (23)	3 (37)
<1/mo	4 (10)	2 (25)
1–4/mo	7 (18)	1 (12)
Many times per week	10 (26)	2 (25)
Daily	4 (10)	0 (0)
Missed activities with friends, no. (%)		
Never	5 (13)	2 (25)
<1/mo	7 (18)	4 (50)
1–4/mo	13 (33)	1 (12)
Many times per week	9 (23)	1 (12)
Daily	4 (10)	0 (0)
STAIC total score, mean (SD)	73.1 (1.9)	71.7 (3.0)
STAIC >68, no.	21	3
CDI score, median (IQR)	9 (7–13)	8 (5–10)
CDI >17, no.	4	0
Area coloured during barostat, median no. pixels (IQR)	18,099 (13,424–32,373)	13,333 (10,481–22,558)
VAS score, mean (SD)	5.2 (0.37)	5.71 (1.2)

IQR = interquartile range; STAIC = State-Trait Anxiety Inventory for Children; SD = standard deviation; CDI = Child Depression Inventory; VAS = visual analog scale.

* Rectal sensory threshold for pain ≤30.8 mmHg (12).

TABLE 4. *Univariate logistic and linear regression of rectal hypersensitivity on the symptom severity variables, anxiety, and depression in the total population*

	Predictive power of the presence of rectal hypersensitivity* (N = 47) OR (95% CI)†
Frequency of pain	5.4 (0.3–97)
Duration of pain ≥1 y	0.6 (0.1–5.2)
Activities at school	1.8 (0.3–9.9)
Activities with friends	3.6 (0.4–33)
Anxiety (STAIC >68)	2.3 (0.4–12)
Depression (CDI >17)	–
	P‡
VAS	0.96
Area coloured during barostat exam	0.30

OR = odds ratio; CI = confidence interval; STAIC = State-Trait Anxiety Inventory for Children; CDI = Child Depression Inventory; VAS = visual analog scale. Insufficient sample size to allow meaningful testing of depression.

* Rectal sensory threshold for pain ≤30.8 mmHg (12).

† Univariate logistic regression.

‡ Linear regression; *P* value of β parameter reported.

missed social activities, VAS and area coloured during the barostat examination), anxiety, or depression.

DISCUSSION

The present study was designed to test the hypothesis that visceral hypersensitivity measured by rectal barostat is associated with symptom severity in children with abdominal pain related to IBS and FAP. In our study, 83% of the children diagnosed with IBS or FAP (as per the Rome II criteria) had a low visceral pain threshold. There was no correlation between visceral hypersensitivity and symptom severity assessed in everyday life or during the barostat examination in our study population. Similarly, there was no relation demonstrated between depression or anxiety and the degree of visceral hypersensitivity, although all of the clinically depressed patients were hypersensitive. These results suggest that the severity of symptoms reported by children with IBS and FAP is poorly explained by RSTP alone, in that increased visceral hypersensitivity was not predictive of increased symptom severity.

Controversy exists regarding the relation in adults between symptom severity and visceral hypersensitivity. Mertz et al (10) reported that the rectal perception threshold is a potential surrogate for IBS symptom severity. However, they used only a visual analog scale for symptom severity estimation. Drossman et al (26) showed a trend for patients with severe functional bowel disorders to have lower rectal sensory threshold, but this achieved statistical significance only with the volume at first pain. Still, other groups clearly have shown that rectal hypersensitivity does not correlate with GI symptom severity reported by adults with IBS (7,27). Similarly, it has been demonstrated recently in a prospective study that IBS symptoms remained stable over 12 months while visceral hypersensitivity improved, suggesting an absence of a direct relation between these phenomena (28). This notion has been suggested in other studies in which clinical improvement was obtained by psychological (27) or pharmacological (29,30) treatments without modification of intestinal sensitivity.

A standardized index is not available for pediatrics, although treatment of adults has validated tools such as the Functional Bowel Disorders Severity Index (31,32). The evaluation of abdominal pain related to FGID in children requires a multidimensional measure (6). Given this, we assessed symptom severity using multiple instruments. The QPGS measured the characteristics of the pain and its consequences on daily living, school absenteeism, and social activity. The latter are good predictors of symptom severity in children because intensity of pain has been shown to be a significant predictor of restriction in daily activities (5). We also measured pain severity during rectal distension to assess the characteristics of the induced pain without recall bias. These parameters have been shown to highly reflect painful symptoms in real life, because the VAS and area coloured during the barostat procedure are correlated with the pain felt at home (12).

It is often said that anxiety and depression are associated with IBS and FAP in adults and children (8,26,33,34) and possibly to contribute to lower scores of quality of life (4). In the present work, 51% of the patients had an anxiety problem, which is consistent with (although a little higher than) that reported in other pediatric and adult studies (8,33,34). However, the degree of anxiety was not correlated with RSTP as found in adults (10). Clinical depression was present in 9% of the patients, all of whom had rectal hypersensitivity. The small number of depressed patients did not allow further testing regarding the relation between depression and RSTP values. Whether depression is a cause or a consequence of the visceral hypersensitivity or a marker of susceptibility for visceral hypersensitivity remains to be elucidated, but abnormalities in serotonin metabolism have been reported in both IBS (35) and depression in adults (36).

The lack of correlation between RSTP and symptom severity may be related to the measurement of the sensory threshold itself. Pain sensation during rectal barostat is a complex phenomenon, and rectal sensory threshold measurement is dependent on 2 components, one physiological (ie, related to the local peripheral mecanoreceptors and afferent nociceptive pathway excitation) (37,38) and the other psychological and cognitive (ie, traits influencing the reporting of pain). The respective role of each component is unknown, although a separate measure of each of them would allow a more precise analysis of their relation with the severity of the symptoms. Our study also is

vulnerable to tertiary center bias. All of the participants were recruited from a tertiary pediatric center; therefore, they may be at the more severe end of the spectrum of FGID disorders. This may have resulted in increased homogeneity of the reported symptoms, making it more difficult to determine associations with other measures, such as RSTP. Concerns regarding the accuracy of retrospective questionnaires in the evaluation of the intensity, frequency, and consequences of pain have been reported (39,40), and also may have modified our findings. The most significant limitation, however, is our sample size; only a moderate to large association between RSTP and symptom severity would have been detectable in this study, primarily because of the paucity of patients diagnosed with FGID having normal rectal sensitivity.

Because we were not able to demonstrate an obvious association between RSTP and symptom severity in children with IBS or FAP, we hypothesize that other factors may play a major role in the severity of the functional intestinal disorders. Mother's IBS status (41), stress (42), comorbid phobic anxiety (15), somatization (43,44), difficulties related to eating (26), more telephone calls to the physician (26), attention to pain (16,45), social threat (16), parental reluctance to accept the diagnosis (46), and family adaptation (17) are factors that have been shown to influence FGID and were not evaluated in this study.

Our results demonstrate that visceral hypersensitivity is a good marker for IBS and FAP in children. Visceral hyperalgesia is central to the physiopathology of abdominal pain in these patients, although it did not explain the severity of GI symptoms in our population. This suggests that other factors—such as familial, psychological, social, and behavioural problems—also contribute to symptom severity in children with FGIDs.

Acknowledgments: We gratefully acknowledge the staff of the Division of Gastroenterology at Hôpital Sainte-Justine. We also thank Lise Giguère, RN, for her technical assistance and Sylvie Marineau for her excellent administrative assistant work.

REFERENCES

1. Caplan A, Walker L, Rasquin A. Validation of the pediatric Rome II criteria for functional gastrointestinal disorders using the Questionnaire on Pediatric Gastrointestinal Symptoms. *J Pediatr Gastroenterol Nutr* 2005;41:305–16.
2. Walker LS, Lipani TA, Greene JW, et al. Recurrent abdominal pain: symptom subtypes based on the Rome II criteria for pediatric functional gastrointestinal disorders. *J Pediatr Gastroenterol Nutr* 2004;38:187–91.
3. Schurman JV, Friesen CA, Danda CE, et al. Diagnosing functional abdominal pain with the Rome II criteria: parent, child, and clinician agreement. *J Pediatr Gastroenterol Nutr* 2005;41:291–5.
4. Youssef NN, Murphy TG, Langseder AL, et al. Quality of life for children with functional abdominal pain: a comparison study of patients' and parents' perceptions. *Pediatrics* 2006;117:54–9.
5. Roth-Isigkeit A, Thyen U, Stoven H, et al. Pain among children and adolescents: restrictions in daily living and triggering factors. *Pediatrics* 2005;115:e152–62.
6. Malaty HM, Abudayyeh S, O'Malley KJ, et al. Development of a multidimensional measure for recurrent abdominal pain in children: population-based studies in three settings. *Pediatrics* 2005;115: e210–5.
7. Schmulson M, Chang L, Naliboff B, et al. Correlation of symptom criteria with perception thresholds during rectosigmoid distension in irritable bowel syndrome patients. *Am J Gastroenterol* 2000;95: 152–6.
8. Di Lorenzo C, Youssef NN, Sigurdsson L, et al. Visceral hyperalgesia in children with functional abdominal pain. *J Pediatr* 2001;139:838–43.
9. Van Ginkel R, Voskuijl WP, Benninga MA, et al. Alterations in rectal sensitivity and motility in childhood irritable bowel syndrome. *Gastroenterology* 2001;120:31–8.
10. Mertz H, Naliboff B, Munakata J, et al. Altered rectal perception is a biological marker of patients with irritable bowel syndrome. *Gastroenterology* 1995;109:40–52.
11. Bouin M, Plourde V, Boivin M, et al. Rectal distention testing in patients with irritable bowel syndrome: sensitivity, specificity, and predictive values of pain sensory thresholds. *Gastroenterology* 2002; 122:1771–7.
12. Faure C, Wieckowska A. Somatic referral of visceral sensations and rectal sensory threshold for pain in children with functional gastrointestinal disorders. *J Pediatr* 2007;150:66–71.
13. Drossman D, Camilleri M, Mayer E, et al. AGA technical review on irritable bowel syndrome. *Gastroenterology* 2002;123:2108–31.
14. Whitehead WE, Palsson OS. Is rectal pain sensitivity a biological marker for irritable bowel syndrome? Psychological influences on pain perception. *Gastroenterology* 1998;115:1263–71.
15. Blomhoff S, Spetalen S, Jacobsen MB, et al. Phobic anxiety changes the function of brain-gut axis in irritable bowel syndrome. *Psychosom Med* 2001;63:959–65.
16. Boyer MC, Compas BE, Stanger C, et al. Attentional biases to pain and social threat in children with recurrent abdominal pain. *J Pediatr Psychol* 2006;31:209–20.
17. Lipani TA, Walker LS. Children's appraisal and coping with pain: relation to maternal ratings of worry and restriction in family activities. *J Pediatr Psychol* 2006;31:667–73.
18. Caplan A, Walker L, Rasquin A. Development and preliminary validation of the Questionnaire on Pediatric Gastrointestinal Symptoms to assess functional gastrointestinal disorders in children and adolescents. *J Pediatr Gastroenterol Nutr* 2005;41: 296–304.
19. Walker L, Caplan-Dover A, Rasquin-Weber A. Manual for the Questionnaire on Pediatric Gastrointestinal Disorders. Nashville, TN: Department of Pediatrics, Vanderbilt University School of Medicine; 2000.
20. Rasquin-Weber A, Hyman PE, Cucchiara S, et al. Childhood functional gastrointestinal disorders. *Gut* 1999;45 (Suppl 2):II60–8.
21. Turgeon L, Chartrand E. Psychometric properties of the French Canadian version of the State-Trait Anxiety Inventory for Children. *Educ Psychol Meas* 2003;63:174–85.
22. Saint-Laurent L. Étude psychométrique de l'Inventaire de dépression pour enfants de Kovacs auprès d'un échantillon francophone. *Can J Behav Sci* 1990;22:377–84.
23. Whitehead WE, Delvaux M. Standardization of barostat procedures for testing smooth muscle tone and sensory thresholds in the gastrointestinal tract. The Working Team of Glaxo-Wellcome Research, UK. *Dig Dis Sci* 1997;42:223–41.
24. Savedra MC, Tesler MD, Holzemer WL, et al. Pain location: validity and reliability of body outline markings by hospitalized children and adolescents. *Res Nurs Health* 1989;12:307–14.
25. Fox M, Thumshirn M, Fried M, et al. Barostat measurement of rectal compliance and capacity. *Dis Colon Rectum* 2006;49:360–70.
26. Drossman DA, Whitehead WE, Toner BB, et al. What determines severity among patients with painful functional bowel disorders? *Am J Gastroenterol* 2000;95:974–80.

27. Poitras P, Riberdy Poitras M, Plourde V, et al. Evolution of visceral sensitivity in patients with irritable bowel syndrome. *Dig Dis Sci* 2002;47:914–20.
28. Naliboff BD, Berman S, Suyenobu B, et al. Longitudinal change in perceptual and brain activation response to visceral stimuli in irritable bowel syndrome patients. *Gastroenterology* 2006;131:352–65.
29. Kuiken S, Tytgat G, Boeckxstaens G. The selective serotonin reuptake inhibitor fluoxetine does not change rectal sensitivity and symptoms in patients with irritable bowel syndrome: a double blind, randomized, placebo-controlled study. *Clin Gastroenterol Hepatol* 2003;1:219–28.
30. Tack J, Broekaert D, Fischler B, et al. A controlled crossover study of the selective serotonin reuptake inhibitor citalopram in irritable bowel syndrome. *Gut* 2006;55:1095–103.
31. Drossman DA, Li Z, Toner BB, et al. Functional bowel disorders. A multicenter comparison of health status and development of illness severity index. *Dig Dis Sci* 1995;40:986–95.
32. Bijkerk CJ, Wit NJ, Muris JWM, et al. Outcome measures in irritable bowel syndrome: comparison of psychometric and methodological characteristics. *Am J Gastroenterol* 2003;98:122–7.
33. Lembo T, Naliboff B, Munakata J, et al. Symptoms and visceral perception in patients with pain-predominant irritable bowel syndrome. *Am J Gastroenterol* 1999;94:1320–6.
34. Hyams JS, Burke G, Davis PM, et al. Abdominal pain and irritable bowel syndrome in adolescents: a community-based study. *J Pediatr* 1996;129:220–6.
35. Coates MD, Mahoney CR, Linden DR, et al. Molecular defects in mucosal serotonin content and decreased serotonin reuptake transporter in ulcerative colitis and irritable bowel syndrome. *Gastroenterology* 2004;126:1657–64.
36. Ebmeier KP, Donaghey C, Steele JD. Recent developments and current controversies in depression. *Lancet* 2006;367:153–67.
37. Aziz Q, Thompson DG. Brain-gut axis in health and disease. *Gastroenterology* 1998;114:559–78.
38. Van Oudenhove L, Demyttenaere K, Tack J, et al. Central nervous system involvement in functional gastrointestinal disorders. *Best Pract Res Clin Gastroenterol* 2004;18:663–80.
39. van den Brink M, Bandell-Hoekstra EN, Abu-Saad HH. The occurrence of recall bias in pediatric headache: a comparison of questionnaire and diary data. *Headache* 2001;41:11–20.
40. Irvine EJ, Whitehead WE, Chey WD, et al. Design of treatment trials for functional gastrointestinal disorders. *Gastroenterology* 2006;130:1538–51.
41. Levy RL, Whitehead WE, Walker LS, et al. Increased somatic complaints and health-care utilization in children: effects of parent IBS status and parent response to gastrointestinal symptoms. *Am J Gastroenterol* 2004;99:2442–51.
42. Chang L, Toner BB, Fukudo S, et al. Gender, age, society, culture, and the patient's perspective in the functional gastrointestinal disorders. *Gastroenterology* 2006;130:1435–46.
43. Walker LS, Garber J, Greene JW. Somatization symptoms in pediatric abdominal pain patients: relation to chronicity of abdominal pain and parent somatization. *J Abnorm Child Psychol* 1991;19:379–94.
44. Robins PM, Glutting JJ, Shaffer S, et al. Are there psychosocial differences in diagnostic subgroups of children with recurrent abdominal pain? *J Pediatr Gastroenterol Nutr* 2005;41:216–20.
45. Walker LS, Williams SE, Smith CA, et al. Parent attention versus distraction: Impact on symptom complaints by children with and without chronic functional abdominal pain. *Pain* 2006;122:43–52.
46. Lindley KJ, Glaser D, Milla PJ. Consumerism in healthcare can be detrimental to child health: lessons from children with functional abdominal pain. *Arch Dis Child* 2005;90:335–7.