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Depression and Somatization Are Associated With Increased Postprandial Symptoms in Patients With Irritable Bowel Syndrome

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BACKGROUND & AIMS: Patients with irritable bowel syndrome (IBS) have increased postprandial symptom responses and more psychosocial morbidities than healthy individuals. However, the relationship between psychosocial status and postprandial symptom responses in patients with IBS is unclear. We investigated this relationship in a prospective study of patients with IBS. **METHODS:** A total of 193 IBS patients, diagnosed according to Rome II (n = 126) or Rome III (n = 67) criteria, consumed a standard breakfast (540 kcal: 36% fat, 15% proteins, 49% carbohydrates, and 8.9 g fiber). They completed visual analogue scales assessing the severity of 5 gastrointestinal symptoms (abdominal pain, bloating, nausea, gas, and fullness) before breakfast and every 30 minutes, up to 240 minutes after eating. All patients completed validated self-report questionnaires for their current levels of anxiety and depression; patients diagnosed based on Rome II criteria also completed a somatization questionnaire. The relationship between these variables and the course of gastrointestinal symptom scores over time was analyzed using linear mixed models, controlling for comorbid functional dyspepsia. **RESULTS:** We observed a main effect of anxiety levels on fullness and bloating ($P < .04$), and of depression levels on abdominal pain ($P = .007$), reflecting a general upward shift of the entire symptom curve. Depression-by-time interactions were seen for nausea and gas ($P < .03$). Somatization levels had a main effect on all 5 symptoms ($P < .0001$), independent of anxiety and depression. We observed somatization-by-time interaction effects for bloating ($P = .005$), and nausea ($P = .02$), and a nonsignificant trend was found for pain ($P = .054$), reflecting a steeper early postprandial increase in symptoms among subjects with higher levels of somatization. **CONCLUSIONS:** Based on a prospective study of patients with IBS, psychosocial morbidities are associated with increased levels of gastrointestinal symptoms in general. Depression and somatization levels are associated specifically with increased postprandial symptoms.

Keywords: Psychologic Factors; Discomfort; Psychiatric; Nervous System.

Irritable bowel syndrome (IBS) is defined by the Rome III criteria as "a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit, and with features of disordered defecation."[1] Despite its high global prevalence (11.2%),[2] IBS remains a poorly understood condition with a multifactorial and heterogeneous etiology and pathogenesis.[3,4] IBS is characterized by high levels of psychiatric comorbidity, particularly anxiety, depressive, and somatoform disorders.[5–7]

A majority of IBS patients perceive their symptoms as being related to meal intake.[8] Perceived intolerance to specific foods also is common but has been shown to correspond poorly with malabsorption testing.[9–11] We recently showed that IBS patients, compared with healthy controls, show increased gastrointestinal (GI) symptom responses to a standard breakfast during a 4-hour postprandial period, particularly for bloating.[12] Altered postprandial small-bowel[13] and colonic[14,15] motor responses as well as malabsorption of certain nutrients,[16] altered colonic fermentation,[17] and/or abnormal gas production or handling[18] all have been suggested to be involved. Taken together, this suggests that meal intake may interact with GI sensory and motor (dys)functions involved in IBS pathophysiology, but the exact mechanisms underlying this phenomenon remain unclear. This represents a huge gap in IBS research given the high prevalence of postprandial exacerbations of IBS symptoms, and the difficulties in managing these symptoms.[8]

However, because IBS should be regarded as a disorder of the brain–gut axis,[19] postprandial symptom responses should be looked at within the context of gut–brain signaling. More specifically, altered central processing and modulation of (nutrient-related) visceral sensory signals also may contribute to the increased postprandial symptom generation found in IBS. Although unexplored, this represents a plausible mechanism because increasing levels of psychological distress are risk factors to develop IBS[20,21] as

Abbreviations used in this paper: **ANS, autonomic nervous system; CCK, cholecystokinin; FD, functional dyspepsia; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-C, constipation-predominant irritable bowel syndrome; IBS-D, diarrhea-predominant irritable bowel syndrome; IBS-SSS, IBS severity scoring system; PHQ, Patient Health Questionnaire; PYY, peptide tyrosine tyrosine.**

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well as associated with increasing GI symptom levels in general (ie, regardless of their timing relative to meal intake) in IBS patients.[22,23] These associations can be explained by the fact that processing and modulation of visceral sensory signals is influenced heavily by psychosocial factors.[24] However, our understanding of the relationship between levels of psychological symptoms and postprandial sensations or symptoms in IBS is incomplete.

The aim of this study therefore was to study the relationship between anxiety, depression, and somatization levels on the one hand and GI symptom levels before and after a standard breakfast on the other hand, in IBS patients. We hypothesized that the severity of anxiety, depression, and somatization symptoms would be associated with increased GI symptom levels at the preprandial baseline, as well as an increased postprandial symptom response.

Materials and Methods

Subjects

We prospectively included patients fulfilling Rome II[25] and later Rome III[1] criteria for IBS, who consulted at a single secondary/tertiary care outpatient unit (Sahlgrenska University Hospital, Gothenburg, Sweden) during the time period from 2005 until 2008. A proportion of the subjects (n = 67) also were included in our recent publication on postprandial symptom response in IBS patients vs controls.[12]

The diagnosis was based on a typical clinical presentation and additional investigations if considered necessary on clinical grounds. However, all subjects underwent a physical examination as well as routine laboratory blood testing including transglutaminase antibodies for celiac disease.

The fact that not all patients were diagnosed according to the same version of the diagnostic criteria rendered subdividing patients according to bowel habits difficult. However, we subdivided the entire patient sample (Rome II and Rome III subgroups combined) into 3 categories based on Bristol Stool Form data: constipation-predominant IBS (IBS-C), diarrhea-predominant IBS (IBS-D), and IBS-nonCnonD (corresponding to Rome II IBS-A [alternating IBS][25] and Rome III IBS-M [mixed IBS] and IBS-U [unsubtyped IBS][1]).

All patients were given study-specific verbal and written information before giving their written consent to participate in the studies. The Regional Ethical Review Board in Gothenburg approved the study before the start of patient inclusion.

Standard Breakfast and Postprandial Symptom Response Assessment

The procedure was described in detail in our previous publication.[12]

All medications with known effects on the gastrointestinal tract were discontinued at least 48 hours before the study, including antidepressants. None of the included subjects were on anxiolytics, and the number of patients on antidepressants was small (<20 patients). After an overnight fast, the subjects presented to the laboratory at 7.30 am. Demographic data including height and weight were collected to calculate body mass index. Subjects were served a breakfast of oat bran (27 g) with 50 g applesauce and 2 dL milk, 2 crispbreads with 10 g margarine and 2 slices of cheese (20 g), and 1 dL apple juice (540 kcal; 36% fat, 15% proteins, 49% carbohydrates, and 8.9 g fiber).

Subjects were instructed to ingest the entire meal and finish within 10 minutes. Gastrointestinal symptoms (abdominal pain, bloating, nausea, gas, and fullness) were assessed before breakfast (preprandial baseline) and every 30 minutes up to 240 minutes postprandially using 100-mm visual analogue scales ranging from no sensation to very severe sensation. Before the meal, all patients completed questionnaires to assess anxiety, depression, somatization, IBS symptoms, and comorbid functional dyspepsia (see later).

Psychosocial Assessment

For the assessment of anxiety and depression symptom levels during the past week, patients completed the validated Hospital Anxiety and Depression Scale.[26] The Hospital Anxiety and Depression Scale consists of 14 items in total (7 anxiety items and 7 depression items), each scored on a Likert scale ranging from 0 to 3. Subscale scores for anxiety and depression are calculated by summing the 7 respective items.

Somatization (the tendency to report multiple somatic symptoms) during the past 4 weeks was assessed using the somatic symptom severity module of the Patient Health Questionnaire (PHQ), consisting of the 15 most common somatic symptoms (PHQ-15).[27] The severity of each of these symptoms and their associated distress is scored on a Likert scale ranging from 0 to 2, resulting in a total somatization score ranging from 0 to 30. To avoid confounding of the relationship between somatization and our GI symptom outcome variables as well as with the comorbid functional dyspepsia (FD) variable (see later) by the GI items of the PHQ-15, these 3 items were omitted as previously described and validated (PHQ-12).[28] Because to the best of our knowledge no validated cut-off values for the PHQ-12 exist, we also report the PHQ-15 scores for descriptive purposes. Somatization was measured only in the Rome II subsample (n = 127; 65.3%).

IBS Symptom Severity and Comorbid Functional Dyspepsia Assessment

All patients also completed the IBS severity scoring system (IBS-SSS).[29] This is a well-validated IBS symptom score that is based on 5 items (severity of pain, duration of pain, abdominal distension, bowel dissatisfaction, and interference with life in general) and uses visual analogue scales. The maximum score is 500 and patients can be categorized as having mild (75–175), moderate (176–300), or severe (>300) IBS.

Comorbid FD was assessed by Rome II[30] or Rome III[31] modular questionnaires, depending on the time of recruitment (before or after the publication of Rome III criteria) yielding information on the presence (yes/no) of comorbid FD.

Statistical Analysis

SAS 9.3 software (SAS Institute, Cary, NC) was used to analyze the data, which are expressed as means ± SEM. Significance was set at a P value of less than .05.

To test our hypothesis that levels of psychological symptoms (anxiety, depression, and somatization) are associated with an increased postprandial symptom response in IBS patients, we used marginal linear mixed models with main effects