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Psychosocial predictors of self-reported fatigue in patients with moderate to severe irritable bowel syndrome

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Abstract

The objective of this study was to assess the level, impact, and predictors of fatigue in patients with moderate to severe irritable bowel syndrome (IBS). One hundred seventy five patients meeting Rome III criteria for IBS completed a variety of measures including the vitality scale of the SF-12, IBS-Symptom Severity Scale, IBS-QOL, Brief Symptom Inventory-18, Screening for Somatoform Symptoms (SOMS-7), and a semi structured clinical interview (IBS-PRO) as part of a pretreatment evaluation of an NIH funded clinical trial of cognitive behavior therapy for IBS. Fatigue was the third most common somatic complaint, reported by 61% of the patients. Levels of fatigue were associated with both somatic (more severe IBS symptoms, greater number of unexplained medical symptoms), behavioral (frequency of restorative experiences) and psychological (e.g., trait anxiety, depression) outcomes after holding constant confounding variables. The final model in multiple regression analyses accounted for 41.6% of the variance in self-reported fatigue scores with significant predictors including anxiety sensitivity, perceived stress, IBS symptom severity, restorative activities and depression. The clinical implications of data as they relate to both IBS and CBT in general are discussed in the context of attention restoration theory.

Keywords

Stress; Attention; Restorative environments; Anxiety sensitivity; Comorbidity; Depression; Quality of life

Introduction

Irritable bowel syndrome (IBS) is a chronic gastrointestinal (GI) disorder characterized by recurrent abdominal pain and bowel disturbance (diarrhea and/or constipation) without obvious structural abnormalities, detected through endoscopy or X ray (Mayer, 2008). Lacking a biomarker that reliably corresponds to GI symptoms, IBS is best understood as a functional illness (i.e., the problem is in the way the intestinal tract functions) whose onset, trajectory and impact are influenced by psychological, physiological, and environmental factors (Tanaka, Kanazawa, Fukudo, & Drossman, 2011). The interplay of these factors has the potential to disrupt brain–gut interactions and gives expression to GI symptoms. It is

believed that the effect of psychosocial factors is strongest in severely affected IBS patients (Lackner, Gudleski, et al., 2012). With a worldwide prevalence of 10–15% (Lovell & Ford, 2012), IBS is more common than diabetes, asthma, heart disease, or hypertension (Adams & Benson, 1990). Not surprisingly, IBS is one of the most common diseases seen in primary care and specialty GI practices (Mayer, 2008). Because IBS symptoms are painful, emotionally bothersome, intrusive and mimic symptoms of organic GI diseases, IBS results in significant direct (e.g., use of healthcare-related services such as physician visits, diagnostic tests, and prescription or over the- counter medication) and indirect (work absenteeism, diminished quality of life) costs to patients, the health care industry and employers (Spiegel, 2013).

Compounding the social and economic costs of IBS are the high rates of co-occurring medical problems. A large comorbidity study of patients with IBS, inflammatory bowel disease and healthy controls demonstrated that IBS patients had a median odds ratio of 1.93 of having a symptom-based non-gastrointestinal somatic diagnosis (Whitehead et al., 2007). Indeed, the biggest driver of health care costs of IBS patients are non-GI symptoms (Levy et al., 2001). A common physical symptom is fatigue (Simren, Abrahamsson, Svedlund, & Bjornsson, 2001). Fatigue can be conceptualized (Grandjean, 1968) along a continuum from extreme tiredness, exhaustion, or a need to rest to high energy, strength, vitality, and enthusiasm (Grandjean, 1968). Fatigue differs from normal tiredness in that it is neither relieved by rest or sleep nor does it correspond to one's level of exertion. Previous research has identified fatigue and loss of energy as important health problems in patients with IBS (Gralnek, Hays, Kilbourne, Naliboff, & Mayer, 2000; Labus, Mayer, Chang, Bolus, & Naliboff, 2007; Mayer, 2000). In a large group of IBS patients, fatigue predicted both physical and mental aspects of quality of life as measured by the SF 36 Health Survey (Spiegel et al., 2004). That said, little is known about the different dimensions of fatigue (e.g., frequency, impact) or how they relate to other aspects of IBS such as GI symptoms, mental well-being, IBS specific quality of life, interpersonal relationships (e.g., negative interactions with others), cognitive style (e.g., anxiety sensitivity, catastrophizing) or activity level. Nor is it clear what other factors predict excessive fatigue in IBS patients. Understanding the predictors of a clinically meaningful problem like fatigue is important because this information may help promote the development of more effective behavioral symptom self-management strategies that, in the absence of a satisfactory medical treatment, could relieve the day to day burden of IBS.

A more complete understanding of the nature and clinical significance of a “nonspecific” symptom like fatigue requires clarifying whether it is a separate and distinct symptom or secondary to any number of medical or mental disorders that are comorbid with IBS *and* characterized by fatigue/loss of energy. It possible that complaints of fatigue are simply due to co-existing depression which affects approximately 20% of IBS patients (Blanchard, 2000). If so, then the magnitude of the observed relationship between fatigue and depression (Asare et al., 2012) may reflect the degree of statistical overlap (i.e., multicollinearity) between the items used to measure both constructs and not a clinically meaningful phenomenon. Multicollinearity is an important but often overlooked methodological issue that arises when two (or more) related variables provide redundant information; that is, constructs are described as conceptually different but tap the same underlying variable. A similar problem applies to the relationship between fatigue and somatization. It is unknown whether unexplained fatigue is part of a set of medically benign symptoms that are reported by somatizing patients who express emotional distress in the form of physical complaints. The aims of this study were to examine the level of fatigue perceived by more severely affected IBS patients and to explore the potential factors influencing fatigue and its relationship to other aspects of IBS.

Method

Participants

Participants included 176 consecutively evaluated IBS patients recruited primarily through local media coverage and community advertising and referral by local physicians to a tertiary care center at 2 academic medical centers. To qualify, participants must have met Rome III IBS diagnostic criteria (Drossman, Corazziari, Talley, Thompson, & Whitehead, 2000) without organic gastrointestinal disease (e.g., IBD, colon cancer, etc) as determined by a board-certified study gastroenterologist. Rome criteria define IBS as recurrent abdominal pain or discomfort at least 3 days per month over the last 3 months that is associated with at least 2 of the following: 1) improvement with defecation, 2) onset associated with a change in stool form, or 3) onset associated with a change in the frequency of stool (Drossman, Corazziari, Talley, Thompson, & Whitehead, 2006). Because this study was conducted as part of a clinical trial for moderate to severely affected patients with IBS (Lackner, Keefer, et al., 2012), participants must have also reported IBS symptoms of at least moderate intensity, symptoms occurring at least twice weekly for 6 months *and* causing life interference. Institutional review board approval and written, signed consent were obtained before the study began. This study was completed in full compliance with the Declaration of Helsinki.

Procedure

After a brief telephone interview to determine whether participants were likely to meet basic inclusion criteria, participants were scheduled for a medical examination to confirm IBS diagnosis (Drossman, Corazziari, et al., 2000; Longstreth et al., 2006) and psychometric testing, which for the purposes of this study included the test battery described below.

Assessment measures

Fatigue—The primary unit of analysis for statistical analyses was based on the vitality scale of the SF-12 Health Survey (Ware, Kosinski, & Keller, 1996). The SF-12 contains 12 items from the SF-36 Health Survey, a generic measure of quality of life that measures eight domains of health: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health. The SF-12 vitality scale requires respondents to indicate how much of the time during the past four weeks they had a lot of energy. Possible responses ranged from 1 (all of the time) to 6 (none of the time) with lower score indicating higher vitality (greater energy/lower fatigue).

In addition to measuring fatigue intensity, we were interested in describing the clinical significance of reported self-reported fatigue as measured by the Patient Reported Outcomes Interview for the Functional Gastrointestinal Disorders: IBS Module (IBS-PRO, Keefer, Lackner, & Brenner, 2009). The IBS-PRO is a clinician administered structured interview that assesses the frequency and impact of individual IBS symptoms as specified by Rome criteria. For each item, standardized questions and probes are provided. The measure contains separate 0–4 frequency and impact scales. Consistent with Rome criteria, the IBS PRO assesses symptoms over the past 3 months. The structure and format of the IBS-PRO is based on other semi structured instruments (Blake et al., 1995) that gauges clinical significance with reference to specific dimensions that are regarded as important to describing symptom severity (i.e., frequency, subjective distress, functional impairment). Frequency ratings are based on the percent of time the symptom has occurred over the past 3 months from the patient's perspective. Frequency percentages correspond one of five adjectival descriptors (e.g., 25% correspond with the "sometimes" descriptor) defined by previous IBS researchers (Drossman, Corazziari, Delvaux, et al., 2006). A second rating is

made for the impact of symptom based on the patient's level of distress and/or impairment due to symptoms. Ratings are made on a scale with brief descriptors attached to each of the five scale values. Symptoms can thus have individual scales ranging from 0-0, 1-1, 1-2, 2-1, 2-2, 1-3, up to 4-4, with the first digit of the number pair representing the frequency and the second digit representing the impact of symptom. A symptom registers as clinically meaningful if it meets the "rule of three" – that is, the sum of frequency and impact yields a score of three or greater. IBS PRO data were used for descriptive purposes and not included in analyses (e.g., correlations, regression analyses).

IBS symptom severity—The Irritable Bowel Syndrome Symptom Severity Scale (IBS-SSS; Francis, Morris, & Whorwell, 1997) is a 5-item instrument used to measure severity of abdominal pain, frequency of abdominal pain, severity of abdominal distension, dissatisfaction with bowel habits, and interference with quality of life, each on a 100-point scale. For four of the items, the scales are represented as continuous lines with endpoints 0% and 100%, with different descriptors at the endpoints and adverb qualifiers (e.g., "not very," "quite") strategically placed along the line. Respondents mark a point on the line between the two endpoints reflecting the extremity of their judgment. The proportional distance from zero is the score assigned for that scale (hence scores range from 0 to 100). The endpoints for the severity items are "no pain" and "very severe," for satisfaction, the endpoints are "not at all satisfied" and "very satisfied," and for interference they are "not at all interferes" to "completely interferes." A final item asks the number of days out of 10 the patient experiences abdominal pain and the answer is multiplied by 10 to create a 0 to 100 metric. The items are summed and thus the total score can range from 0 to 500.

Quality of life—The IBS-QOL (Drossman, Patrick, et al., 2000) is a 34-item measure constructed specifically to assess the subjective well-being of patients with IBS. Each item is scored on a five-point scale (1 = not at all, 5 = a great deal) that represents one of eight dimensions (dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual dysfunction, and relationships). Items are scored to derive an overall total score of IBS related quality of life. To facilitate score interpretation, the summed total score is transformed to a zero to 100 scale ranging from zero (poor quality of life) to 100 (maximum quality of life). IBS-QOL has good reliability (Cronbach's alpha = .95), convergent validity and construct validity (Drossman, Patrick, et al., 2000) and sensitivity to change following CBT of different "dosages" (Lackner et al., 2008).

Perceived Stress Scale (PSS)—The PSS measures the degree to which situations in one's life are appraised as stressful (Cohen, Kamarck, & Mermelstein, 1983). The 4 item version of the PSS (Cohen & Williamson, 1988) was used. Its items are designed to tap the degree to which respondents find their lives uncontrollable, unpredictable and overloading. These three factors have been consistently found to be central components of the stress experience. Item are rated on a 5 point Likert scale ranging from 0 (never) to 4. The PSS-4 shows adequate reliability with a Cronbach's alpha of .85 as well as acceptable correlations with measures of conceptually congruent constructs (Cohen et al., 1983).

Abdominal pain—Abdominal pain intensity over the previous 7 days was measured with an 11-point numerical rating scale (PI-NRS), where 0 = no pain and 10 = worst possible pain (Turk et al., 2006). Patients circled the number from 0 to 11 that best described their average abdominal pain over the past 7 days. This pain measure is widely used and recommended in studies of patients with IBS (M. P. Jensen, Karoly, & Braver, 1986).

Pleasant activities—The Pittsburgh Enjoyable Activities Test scale (PEAT) (Pressman et al., 2009) is a 10 item scale that assesses the frequency of involvement in a spectrum of

leisure activities associated with feelings of renewed energy, concentration and mental clarity. The ten items include: spending quiet time alone; spending time unwinding; visiting others; eating with others; doing fun things with others; club, fellowship and religious group participation; vacationing; communing with nature; sports; and hobbies. These activities are believed to enhance well-being by acting as breathers, restorers and stress buffers.

Instructions for the PEAT were: "We are interested in how often in the last month you were able to spend time in activities that you enjoyed. Over the past month, how often have you been able to spend time doing the following?" Response options ranged from "Never" (0 point) to "Every Day" (4 points) and "Not Applicable/Do Not Enjoy" (0 point). The PEAT was scored as the sum of all items (maximum = 40).

Depression—Depressive symptoms were measured using the depression scale of the 18 item version of the Brief Symptom Inventory (Derogatis, 2000). The scale includes 5 items rated on a 5 point scale (0- not at all, 1, a little bit, 3 = quite a bit, 4 = extremely) to reflect respondents' distress about depressive symptoms (e.g., feeling lonely, blue, worthless, hopeless). The BSI has been used extensively in IBS research (Dorn et al., 2007). Internal consistency, test-retest reliability, and validity of the BSI-18 are well established (Derogatis, 2000).

Somatization—Somatization was measured using the Screening for Somatoform Symptoms-7 (SOMS-7, Rief & Hiller, 2003). The SOMS includes a total of 53 physical symptoms, drawn from the DSM-IV (American Psychiatric Association, 1994) and the International Classification of Diseases (ICD-10) definitions for somatization disorder and somatoform autonomic dysfunction. Subjects are instructed to report only complaints for which physicians have found no currently physical pathological cause. Respondents are asked (Rief & Hiller, 2003) to report the symptoms that have been present during the past 7 days. The total number of endorsed symptoms yields a somatization symptom count which has been found to discriminate patients with somatoform disorders from those with other forms of mental disorders. To avoid collinearity problems, we excluded the fatigue item when calculating the somatization. The SOMS-7 has demonstrated high internal consistency (Cronbach's $\alpha = .92$), reasonable test-retest reliability ($r = .76$) and high associations with a number of somatoform disorders (Rief & Hiller, 2003).

Anxiety—Trait anxiety was measured using the abbreviated Trait subscale of the STAI (Spielberger, 1995). In responding to the 10 items of the T-Anxiety scale, subjects indicate how they generally feel by rating the frequency of their feelings of anxiety on a 4-point scale ranging from 1 (almost never) to 4 (almost always). A wide body of research supports the construct validity, test-retest reliability, and reliability of the STAI (Spielberger, 1989).

Interpersonal functioning—Interpersonal functioning was measured with the Negative Interactions Scale (NIS). The NIS assesses social encounters and interactions that are characterized by conflict, excessive demands and/or criticism (30, 31). Our version of the NIS includes 5 items that assess the frequency (ranging from 1 = never to 4 = very often) of negative social exchanges with a spouse, family members, friends, neighbors, in-laws. The scale includes four items from the original 4-item scale developed and validated by Krause and one additional item drawn from Schuster, Kessler, and Aseltine (1990) ("How often do they let you down when you are counting on them?") and used in the MIDMAC (MacArthur Foundation Research Network on Successful Midlife Development). Participants were asked "In the past month, how often have others..." about exchanges such as "... made too many demands on you?", "...been critical of you?", "... pried into your affairs?", "...taken advantage of you?" and "...let you down when you were counting on them?" High scores suggest that respondents engage in negative interactions more frequently. The five item NIS

is part of the assessment battery for social/environmental burdens of the Pittsburgh Mind Body Center, a joint research project of the University of Pittsburgh and Carnegie Mellon University.

Pain catastrophizing—The two item version of the catastrophizing subscale of the Coping Strategies Questionnaire (Jensen, Keefe, Lefebvre, Romano, & Turner, 2003) asks patients to rate the frequency with which they engage in thoughts that index catastrophizing during pain episodes (e.g., “When I am in pain, I feel I can’t stand it anymore). Respondents rate each item using a scale ranging from 0 (never do) to 7 (always do).

Anxiety Sensitivity Inventory—The ASI (Peterson & Reiss, 1993) is a self-report measure that reflects fear of anxiety (e.g., “It scares me when I am anxious”), arousal related bodily sensations (“It scares me when my heart beats rapidly”) and their consequences (e.g., “When I notice my heart is beating rapidly, I worry that I might have a heart attack”). Each of the 16 items of the ASI is rated on a six point scale (0 = very little, 5 = very much). In addition to a total score, the ASI yields three empirically derived subscales relating to fear of publicly observable anxiety reactions (e.g., fear of trembling arising from beliefs that trembling will be negatively evaluated), fears of somatic symptoms (e.g., It scares me when my heart beats rapidly”, and fears of cognitive dyscontrol (fear of concentration difficulties arising from beliefs that such difficulties have catastrophic consequences). The ASI has demonstrated sound psychometric properties in both clinical and nonclinical samples, including high internal consistency (α .80 to .90; (Peterson & Reiss, 1993; Taylor, 1999; Telch, Shermis, & Lucas, 1989).

Medical comorbidity—Because poor physical health may impact energy/fatigue, nonpsychiatric medical comorbidity was assessed using a modified version of the survey used in the National Health Interview Survey (NHIS) to record the recency of commonly occurring chronic conditions believed to be associated with substantial quality of life impairment (Schoenborn, Adams, & Schiller, 2003). We have adapted the NHIS checklist to characterize physical comorbidity of IBS patients in three NIH funded clinical trials (Lackner et al., 2006). The current version (Lackner, Brenner, & Keefer, 2009) covers 112 medical conditions organized around 12 body systems (musculoskeletal, digestive, kidney/genitourinary, endocrine, respiratory, circulatory, cardiovascular, oral, CNS, dermatological, Ear Nose, Throat [ENT], cancer). Respondents were asked whether a doctor had ever diagnosed them with a condition and, if so, whether the condition was present in the past 3 months. Persons were counted as current cases if the diagnosed condition was reported as present in the last 3 months. The checklist was constructed to capture information about the most common comorbidities in the general population, those believed to occur frequently in IBS patients, those regarded as most important to IBS patients and those regarded as most important in existing comorbidity measures (Charlson, Pompei, Ales, & MacKenzie, 1987). A total comorbidity score was based on the number of medical comorbidities a patient reported as present over the previous 3 months. Evidence for the discriminant and convergent validity comes from correlation analyses showing that number of medical comorbidities is associated with physical (–.41) but not mental aspect of quality of life as assessed with the SF 36 Healthy Survey (Lackner, Ma, et al., in press).

Data analyses plan

Data analyses were carried out in three steps. The first step was to characterize the sample using means, standard deviations or percentages. At the second step, we conducted partial correlations to describe the relationship between each clinical variable after holding constant potentially confounding variables including age, education, income, marital status, IBS subtype and duration of symptoms. Because correlations do not account for overlap among

variables, the third step involved multiple regression analyses to determine the proportion of variance in fatigue accounted for by a combination of demographic, psychosocial, and somatic variables.

Results

Characteristics of the sample

Table 1 displays the demographic and clinical characteristics of the sample. The sample was predominately young, educated, female and chronically ill (average duration of IBS symptoms = 16.5 years). The mean total score on the IBS-SSS for the sample falls in the high moderate range of IBS symptom severity (moderate = 176–300; severe > 300). Patients' average abdominal pain intensity for seven days prior to testing was 5.0 using an 11 point numerical rating scale (0 = No Pain, 10 = Worst Pain Possible). The group mean for the IBSQOL was 56.0 which suggest that our cohort had significant quality of life impairment due to IBS symptoms (Patrick, Drossman, & Frederick, 1997). Twenty percent of subjects had a *T*score of 63 or higher (on the community norm) on the General Severity Index which summarizes overall level of psychological distress based on responses to the Anxiety, Depression, and Somatization subscales of the BSI.

Based on responses to the IBS-PRO, fatigue was a common, distressing, and disabling somatic complaint. On the IBS-PRO, 70.5% of patients reported fatigue that occurred at least 50% of the time over the previous 3 months. Sixty one percent of the patients indicated that fatigue was at least a moderate (i.e., distress clearly present but still manageable with some disruption of specific daily activities due to fatigue) source of distress and/or life interference. Fatigue registered as a clinically meaningful (i.e., satisfied the rule of three) in 60.8% of our patients (*N* = 107). Of 14 symptoms, fatigue was the third most severe symptom. Fig. 1 presents the severity of symptomatic fatigue in relation to other IBS symptoms assessed with the IBS-PRO.

Associations between clinical variables and fatigue

We conducted a series of partial correlations to assess the magnitude of the relationships between fatigue (as measured with the SF 12 vitality scale) and clinical variables while controlling for possible confounding variables (e.g., demographics, duration of IBS, gender, etc). As shown in Table 2, all significant correlations were in the expected manner. Fatigue was positively associated with both the global severity of IBS symptoms and the number of medically unexplained somatic complaints (i.e., somatization, and negatively associated with the quality of life impairment due to IBS symptoms. Neither the average intensity of abdominal pain nor the number of self-reported medical comorbidities corresponded with fatigue. On the other hand, fatigue was consistently associated with behavioral (participation in restorative leisure activities, PEAT), cognitive (anxiety sensitivity, catastrophizing, perceived stress) and emotional (anxiety, depression) variables. Of psychosocial factors, the strongest correlations with fatigue were the PSS, BSI-Depression, STAI-Trait and the PEAT. That is, patients with higher levels of fatigue reported more stress, depression, and trait anxiety *and* less frequent participation in pleasurable activities. Fatigue levels were positively and significantly associated with cognitive variables, including anxiety sensitivity and catastrophizing, although the magnitude of these correlations was slightly lower (range .22–.26) than those with somatic and distress variables (range .28–.45). In general, individuals with greater fatigue perceived their somatic complaints (pain, arousal symptoms) in a more catastrophic manner. With respect to ASI subscales, fatigue was associated with both the fear of physical catastrophe and fear of cognitive dyscontrol (but not the fear of publicly observable reactions scale.

Clinical predictors of fatigue

We conducted multiple linear regressions to identify predictors of fatigue as measured by the SF-12 while controlling for potentially confounding variables. In order to limit the number of variables in the models, only variables that were significantly correlated with fatigue were entered as predictor variables. We also assessed multicollinearity statistics [variance inflation factors (VIF) and tolerance] for the regression analyses because of the strong correlations among many of the predictor variables. Although multicollinearity would not affect the reliability of the whole regression model or blocks of variables entered, it would call into question the validity of the results of individual predictors. VIF values above 10 and tolerance values below .10 usually indicate problems of multicollinearity (Hair, Black, Babin, & Anderson, 2009). Our results showed that the highest VIF was 3.03 and the lowest tolerance value was .33, suggesting that multicollinearity did not compromise the interpretability of the results of the present study since all values well within an acceptable range.

Demographic variables were entered into the regression equation in the first step; somatic variables were entered in the second step; and the third step introduced psychosocial (cognitive, emotional) variables. Entering the variables in steps allows us to determine the incremental variance attributed to each conceptually distinct block of variables. The results of the regression analyses are shown in Table 3. In step 1, being more educated and having more chronic IBS symptoms were significantly related to greater fatigue. As a set, these variables accounted for 12.7% of the variance in fatigue ($F = 3.63, p < .01$). In Step 2, the somatic illness variables explained an additional 10.2% of the variance in fatigue ($F = 9.70, p < .01$). More severe IBS symptoms and greater QOL impairment due to IBS symptoms (emerged as significant predictors of fatigue at step 2. The addition of cognitive and emotional variables at Step 3 explained an additional 18.7% of the variance in fatigue ($F = 3.67, p < .01$). This final model explained 41.6% of the variance in fatigue scores with significant predictors including anxiety sensitivity, perceived stress, IBS symptom severity, restorative activities (PEAT) and depression. The proportion of variance accounted for by education level, duration of symptoms, and IBS-QOL was not significant in the final model.

Conclusion

The present study sought to assess the psychosocial correlates and predictors of fatigue in a sample of patients with moderate to severe IBS patients treated in the context of an NIH funded clinical trial of CBT for IBS. Our data underscore the importance of fatigue as a major somatic complaint of IBS patients. As Fig. 1 shows, when we applied the “rule of three” for determining the clinical significance of a symptom, fatigue as measured by the IBS-PRO was reported by 60.8% of the patients at baseline assessment. By comparison, 5–20% of the general population suffers from symptomatic fatigue. The percentage of study patients who reported symptomatic fatigue was comparable to those with loose bowels and was only exceeded by the proportion of patients reporting abdominal pain/discomfort. Because our sample included a greater proportion (43%) of patients with diarrhea predominant IBS, it is possible that the rate of symptomatic loose bowels reflects the composition of our sample. If so, fatigue rivals abdominal pain as one of the more symptoms of IBS. Fatigue was positively and significantly associated with a range of somatic, cognitive, and emotional variables. IBS patients with greater fatigue reported more severe IBS symptoms, greater quality of impairment due to IBS symptoms, more distress (anxiety, depression) and more negatively skewed cognitions than patients with lower levels of fatigue. The two variables unrelated to fatigue were average abdominal pain intensity (past 7 days) and number of medical comorbidities. Psychological factors that predicted fatigue included a combination of behavioral (frequency of participation in restorative activities),

cognitive (anxiety sensitivity), emotional (depression) and somatic (severity of IBS symptoms) variables. These findings underscore the multidimensional nature of fatigue.

Our data are consistent with the broader health literature highlighting the importance of fatigue as a biobehavioral marker of health. Indeed, the World Health Organization identifies “energy and fatigue” as an integral part of general health and determinant of overall quality of life (WHOQOL Group, 1997). The importance of fatigue is echoed by studies (Andersen & Lobel, 1995) that indicate fatigue is one of 4 variables that people use to describe their health status. This finding is important because self-ratings of health are stronger than physician ratings at predicting outcomes such as mortality (Idler & Benyamini, 1997). It is worth considering whether individuals may be more accurate than physicians in judging their health status because of the importance they attach to fatigue (Hewlett et al., 2005; Yorkston, Johnson, Boesflug, Skala, & Amtmann, 2010).

There are several reasons why fatigue is overlooked. First, because fatigue is a subjective experience, its presence relies on self-report which may be dismissed as a perceptual abnormality. Second, while fatigue is experienced by patients with a range of conditions (e.g., renal disease, diabetes, MS, arthritis, cancer, heart disease, back pain) it is with few exceptions (e.g., Chronic Fatigue Syndrome) a nonspecific complaint. This means that fatigue is typically subordinated to the core symptom(s) that prompt patients to seek treatment. Because conventional modes of practice subscribe to disease-specific protocols, “background” symptoms like fatigue are often ignored. Even when fatigue is symptomatic of a given disorder (e.g., depression), it is not typically the focus of treatment. Neither cognitive nor behavioral therapy for depression explicitly targets relief of fatigue. Behavioral models target feelings of dysphoria (Lewinsohn & Amenson, 1978), while cognitive models target self-denigrating thoughts (Beck, Rush, Shaw, & Emery, 1979). Both models presume that relief of the complexion of depression symptoms (e.g., fatigue) will follow changes in mood (sadness, pessimism, dissatisfaction), vegetative symptoms (e.g., changes in sleep, appetite) or cognitive symptoms (guilt worthlessness). While CBT for depression is, in fact, associated with significant changes in fatigue (Mohr, Hart, & Goldberg, 2003), the magnitude of the effect size is rather modest and could be improved by developing more robust behavioral strategies that directly tackle fatigue and its disabling effects. For this to happen, clinicians and researchers need to elevate the importance of fatigue to the level that patients do. Third, unlike somatic symptoms like headaches or abdominal pain, fatigue is neither specific to a class of medical diseases nor a specialty within a branch of medicine (e.g., gastroenterologists, neurologists). The ubiquity of fatigue means that it is the complaint of many and the focus of few. Last, because levels of fatigue are tied to lifestyle factors (e.g., long work days, high-paced lifestyles, overscheduled social calendars, family obligations), it is oftentimes dismissed as a normal part of life much like sleepiness and tiredness. The behavioral, cognitive, and emotional correlates of fatigue in patients of our study suggest that fatigue is hardly a normative experience. It is a clinically meaningful health problem that is for IBS patients in our sample very common, disabling and distressing.

The observed relationship between pleasant activities and fatigue is an interesting finding. An emphasis on pleasurable events is hardly new to the behavioral literature. The behavioral model of depression (Hopko, Lejuez, Ruggiero, & Eifert, 2003) assumes that low rates of reinforcement lead to low rates of initiating behaviors, which in turn led the person to become sad and depressed. Because of the emphasis behavioral models of depression place on reinforcement contingencies, behavioral techniques emphasized the implementation of behavioral-activation procedures (e.g., pleasant events scheduling) aimed at increasing patient activity and access to reinforcement. We are not inclined to believe that reinforcement factors satisfactorily account for the observed relationship between pleasant

activities and fatigue in our sample. For reinforcement factors to play a key role, we would have expected more than 19% of the sample to suffer from what is regarded as clinical levels of depression (BSI Depression *T*Score > 63).

An intriguing alternative model, *attention restoration theory* (ART, Kaplan, 1995), comes from the environmental psychology literature ART and suggests that the relationship between pleasant activities and health outcomes is mediated cognitively by attentional processes. Drawing on William James's notion of 'voluntary attention' (James, 1892), Kaplan emphasizes two type of attention: involuntary attention and directed attention (Berman, Jonides, & Kaplan, 2008). According to ART, directed attention is a mechanism by which individuals purposefully expend mental effort executing tasks. If the demand for directed attention is prolonged, it can become depleted which can cause stress and fatigue. Because indirect attention is held automatically, it is neither inherently stressful nor does it cause the (mental) fatigue associated with prolonged directed attention. Stimuli vary in the extent to which they capture and hold attention effortlessly. Those stimuli that support the experience of involuntary attention are experienced as more restorative and therefore more pleasurable. Activities are more pleasurable because they attract involuntary attention and thus permit depleted attention capacity recovery so that fatigue is reduced.

ART initially focused on activities (e.g., walking or sitting outdoors in more natural surrounding such as a park, garden or near water, tending plants, gardening, bird watching, wildlife, and caring for pets) in the natural environment because it is endowed with four properties deemed inherently restorative or stress-reducing. However, restorative experiences are not necessarily confined to natural surroundings. A number of creative, social, physical, spiritual, reflective, and travel activities have restorative properties (Jansen & von Sadvoszky, 2004). Whether the participation in these restorative activities is associated with measures of positive psychological and physical well-being has received limited attention (Pressman et al., 2009). Our data contributes to the literature by showing that individuals, who participate more frequently in pleasurable activities having restorative qualities report lower levels of fatigue, perceive their lives as less stressful (i.e., overwhelming, uncontrollable), and experience less psychological distress (i.e., anxiety, depression).

The finding that anxiety sensitivity (AS) predicted fatigue is notable. AS is a dispositional, trait-like cognitive characteristic that helps explain why people respond differently to similar anxiety stimuli. AS theory (Taylor, 1999) states that individuals high in AS respond fearfully to anxiety-related bodily sensations associated with autonomic arousal because of their beliefs about the dangerousness of these sensations. For example, a person high in AS fears that a racing heart beat means s/he is likely to have a heart attack. The "high AS" individual is likely to experience elevated levels of anxiety and to be at greater risk for a panic attack and other symptoms of autonomic hyperarousal (e.g., racing heart beat). Empirical support for the AS construct (Olatunji & Wolitzky-Taylor, 2009) has prompted other researchers to explore whether the explanatory value of AS extends to anxiety-mediated physical problems (Asmundson, Kuperos, & Norton, 1997; Carr, Lehrer, Rausch, & Hochron, 1994; Labus et al., 2004). Because of its focus, relatively few efforts have linked AS to physical problems that are not mediated by anxiety or hyperarousal. One exception comes from Fairholme, Carl, Farchione, and Schonwetter (2012) who studied the relationship between AS and fatigue and obtained two important findings relevant to the present study. First, they found that AS was positively and significantly correlated with fatigue such that individuals with more fatigue tended to catastrophize about the consequences of anxiety/arousal symptoms (i.e., high AS). Second, AS moderated the relationship between fatigue and severity of insomnia such that the magnitude of the association between fatigue and insomnia was highest for "high AS" individuals. These are

important findings because fatigue is neither a problem of anxiety nor hyperarousal and therefore it would not necessarily be expected to correlate with AS. It is possible that IBS patients with a strong fear of anxiety/arousal symptoms (higher AS) may contribute to, or amplify, the intensity of somatic sensations (e.g., fatigue) that are not necessarily related to autonomic nervous system arousal (e.g., heart palpitation, shortness of breath). This would differ from anxiety disordered patients (e.g., panic) whose attentional bias for somatic perturbations is specific to autonomic sensations (Pilkington, Antony, & Swinson, 1998). It is also possible that fatigue like other negative moods (Chepenik, Cornew, & Farah, 2007) affects cognitive processes such as anxiety sensitivity. Drawing from the principles of attention restoration theory (Kaplan, 1995), overuse of the capacity to direct attention can distort one's ability to perceive and interpret information. If this includes internal somatic cues, fatigue may increase the likelihood of drawing catastrophic interpretations of benign bodily sensations (i.e., increased anxiety sensitivity).

Results should be interpreted in light of study limitations. Because our data are cross sectional, we do not intend to suggest that the findings demonstrate causal relationships between clinical variables such as restorative experiences, AS or fatigue. At best, our data can be construed as suggestive of a possible causal relationship that could be confirmed through longitudinal analyses with a larger sample. Fatigue intensity was assessed using a single question. A stronger study of a complex construct like fatigue would have used a multi-item instrument in part because they better estimate internal-consistency than single item ones. Single item measures are also problematic because they are rather crude indices of complex constructs like fatigue. While 61% of patients report symptomatic fatigue, it is unclear which aspects of fatigue patients experience. We have discussed our findings in terms of mental fatigue. It is possible that our patients suffered from physical fatigue (as well or instead). Given the proportion (20%) of patients who reported comorbid low back pain, it is possible that they suffered from muscle fatigue. Future research should disentangle fatigue as a manifestation of exhausted feelings of physical exertion in the context of poor physical fitness and/or psychological demands in the context of poor coping. Our decision to focus on fatigue was based on a consistent clinical observation across multiple assessors of different disciplines (psychology, medicine) at two sites of an NIH trial that patients reported self-reported fatigue at a level that rivaled core GI symptoms during baseline screening. This was an unexpected finding and one that merited empirical evaluation with the measurement tools available to us. We believe that the novelty and clinical importance of our study offsets the methodological imperfections of our fatigue measure. Future research combining the strengths of the present study (e.g., formally diagnosed IBS patients, sample size, psychometric soundness of testing battery, sound statistical approach) with a more sophisticated fatigue instrument is needed to build on what we think are promising data about an understudied problem. Because of the relative demographic homogeneity of our select sample of patients enlisted in a behavioral trial (mostly white, female, chronically ill and educated patients seeking non drug treatment), our results may not be generalized to a broader, more diverse population.

In conclusion, excessive fatigue in a sample of severely affected IBS patients was common and associated with significant distress and life interference. These findings suggest that fatigue is a clinically important somatic complaint whose frequency and impact is comparable to (abdominal pain) and exceeds (e.g., stool frequency) core symptoms of IBS. Further research is needed to understand more clearly just how fatigue impacts— and is impacted by— the day to day burden of IBS.

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Abbreviations

SF-36	Short Form-36
SF-12	Short Form-12
IBS PRO	Irritable Bowel Syndrome Patient Reported Outcome
IBS-SSS	Irritable Bowel Syndrome Symptom Severity Scale
IBS-QOL	Irritable Bowel Syndrome Quality of Life
PSS	Perceived Stress Scale
PEAT	Pittsburgh Enjoyable Activities Test
NIS	Negative Interactions Scale
SOMS	Screening for Somatoform Symptoms
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders – IV
STAI	State-Trait Anxiety Inventory
ASI	Anxiety Sensitivity Inventory
BSI-Depression Scale	Brief Symptom Inventory-Depression Scale
ART	Attention Restoration Theory
AS	Anxiety Sensitivity
IBS	Irritable Bowel Syndrome
GI	Gastrointestinal
ICD-10	International Classification of Diseases-10
GERD	Gastroesophageal Reflux Disease

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Fig. 1.

The severity of fatigue in relation to IBS symptoms.

Note. $N = 175$. We converted frequency and impact scores into a dichotomous measure of severity which regards a symptom as significant if its frequency Sometimes (or about 25% of the time)/ Intensity Moderate distress clearly present but still manageable; some disruption of specific daily activities

Table 1Demographic and clinical characteristics ($N = 176$)

	<i>M (SD)</i>	<i>N (%)</i>
Age	41.0 (15.0)	
Gender (% female)		138 (78.4%)
Race (% white)		160 (90.9%)
<i>Education</i>		
High school or less		36 (20.6%)
College degree		75 (42.9%)
Post-college degree		51 (29.1%)
Other		13 (7.4%)
<i>Income</i>		
< 15,000		14 (8.0%)
15,001–30,000		21 (12.0%)
30,001–50,000		35 (20.0%)
50,000–75,000		30 (17.1%)
75,001–100,000		11 (6.3%)
100,001 – 150,000		15 (8.6%)
>150,000		20 (11.4%)
Don't know/Not sure		9 (5.1%)
Prefer not to answer		20 (11.4%)
Duration of sxs (years)	16.5 (14.3)	
<i>IBS Subtype</i>		
IBS-Constipation		46 (26.1%)
IBS-Diarrhea		76 (43.2%)
IBS-Alternating		54 (30.7%)
IBS-SSS	284.7 (76.3)	
IBS-QOL	56.0 (19.3)	
Abdominal pain	5.0 (2.0)	
# Medical comorbidities	4.3 (4.6)	
PEAT	31.7 (6.3)	
BSI-Depression	4.5 (4.8)	
SOMS-7	7.7 (5.7)	
STAI-Trait anxiety	20.7 (6.4)	
NIS	10.3 (3.2)	
Catastrophizing	2.6 (1.7)	
PSS	7.1 (3.4)	
ASI	24.9 (12.0)	
Physical concerns	14.7 (8.0)	
Psychological concerns	7.3 (5.9)	
Social concerns	7.2 (2.4)	
Fatigue	4.1 (1.2)	

Note: Duration sxs = Duration of IBS symptoms; IBS-SSS = IBS Symptom Severity Scale; IBS-QOL = IBS Quality of Life; # Medical Comorbidity = Number of Medical Comorbidities; PEAT = Pittsburgh Enjoyable Activities Test; BSI-Depression = Brief Symptom Inventory-Depression Scale; SOMS7 = Screening for Somatoform Symptoms-7; STAI-Trait = State-Trait Anxiety Inventory–Trait Scale; NIS = Negative Interaction Scale; Catastrophizing = Pain Catastrophizing; PSS = Perceived Stress Scale; ASI = Anxiety Sensitivity Index.

Table 2

Partial correlations between fatigue and independent variables (controlling for confounding variables)

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Fatigue	–												
2. IBS-SSS	.33	–											
3. IBS-QOL	–.40	–.44	–										
4. Abd. Pain	.12	.52	–.26	–									
5. MedCo	.11	.14	–.23	.14	–								
6. PEAT	–.33	–.16	.19	–.14	–.21	–							
7. BSI-Dep	.43	.27	–.45	.11	.28	–.24	–						
8. SOMS-7	.28	.24	–.38	.14	.43	–.18	.41	–					
9. STAI-T	.34	.17	–.45	.09	.18	–.22	.75	.30	–				
10. NIS	.31	.16	–.33	.22	.25	–.16	.62	.33	.51	–			
11. Catast	.22	.42	–.46	.27	.11	–.13	.37	.31	.38	.20	–		
12. PSS	.45	.23	–.45	.16	.27	–.34	.67	.33	.66	.53	.33	–	
13. ASI	.26	.30	–.44	.17	.21	–.08	.61	.41	.58	.41	.45	.49	–

Note: Numbers that are **bolded** are significant at $p < .05$. IBS-SSS = IBS Symptom Severity Scale; IBS-QOL = IBS-Quality of Life; Abd. Pain = Abdominal Pain; Med Co = Number of Medical Comorbidities; PEAT = Pittsburgh Enjoyable Activities Test; BSI-Dep = Brief Symptom Inventory-Depression Scale; SOMS7 = Screening for Somatoform Symptoms-7; STAI-Trait = State-Trait Anxiety Inventory-Trait Scale; NIS = Negative Interaction Scale; Catast = Pain Catastrophizing; PSS = Perceived Stress Scale; ASI = Anxiety Sensitivity Index.

Table 3

Results of multiple linear regressions with fatigue as dependent variable

	Estimate	SE	β	R^2	ΔR^2	Adj. ΔR^2
Step 1				.127	.127	.096
Age	-.01	.01	-.11			
Gender	.01	.21	.01			
Race	-.10	.31	-.03			
Education	-.16	.05	-.28			
Income	-.03	.04	-.08			
Duration Sx	.02	.01	.23			
Step 2				.229	.102	.091
Age	-.01	.01	-.06			
Gender	-.07	.20	-.02			
Race	-.12	.30	-.03			
Education	-.11	.04	-.18			
Income	-.02	.03	-.04			
Duration Sx	.02	.01	.19			
IBS-SSS	.02	.01	.24			
IBS-QOL	-.02	.01	-.21			
Step 3				.416	.187	.154
Age	-.01	.01	-.13			
Gender	-.14	.19	-.05			
Race	-.15	.29	-.04			
Education	-.07	.04	-.12			
Income	-.01	.03	-.02			
Duration Sx	.01	.01	.13			
IBS-SSS	.02	.01	.17			
IBS-QOL	-.01	.01	-.09			
PEAT	-.03	.01	-.16			
SOMS7	.02	.02	.09			
NIS	.03	.03	.08			
Castast.	-.05	.06	-.07			
PSS	.06	.04	.19			
ASI	-.02	.01	-.22			
STAI-Trait	-.01	.02	-.01			
BSI-Dep	.04	.03	.16			

Note: Numbers that are **bolded** are significant at $p < .05$. Duration Sx = Duration of IBS symptoms; IBS-SSS = IBS Symptom Severity Scale; IBS-QOL = IBS Quality of Life; PEAT = Pittsburgh Enjoyable Activities Test; SOMS7 = Screening for Somatoform Symptoms-7; NIS = Negative Interaction Scale; Castast. = Pain Catastrophizing; PSS = Perceived Stress Scale; ASI = Anxiety Sensitivity Index; STAI-Trait = State-Trait Anxiety Inventory-Trait Scale; BSI-Dep = Brief Symptom Inventory-Depression Scale.