

Coping Skills Are Associated With Gastrointestinal Symptom Severity and Somatization in Patients With Irritable Bowel Syndrome



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BACKGROUND & AIMS: Coping resources and processes are altered in patients with irritable bowel syndrome (IBS). We investigated the relationship between coping resources and gastrointestinal (GI) and extra-intestinal symptom severity in patients with IBS and potential mediators of this relationship.

METHODS: We performed a cross-sectional study of 216 patients with IBS attending a secondary/tertiary care specialized outpatient center in Sweden from 2003 through 2007. We collected data on coping resources, levels of anxiety (general and GI specific), depressive symptoms, levels of GI symptoms, and extraintestinal somatic symptoms (somatization) by administering validated self-report questionnaires. General Linear Models were used to assess associations and mediation.

RESULTS: GI symptoms: low levels of physical coping resources (practice of activities that are beneficial for health; $P = .0016$), high levels of general anxiety symptoms ($P = .033$), and GI-specific anxiety symptoms ($P < .0001$), but not depressive symptoms ($P = .89$), were independently associated with GI symptom levels ($R^2 = 0.31$). Anxiety and GI-specific anxiety partially mediated the effect of physical coping. Somatization: low levels of physical coping resources ($P = .003$), high levels of anxiety ($P = .0147$), depressive ($P = .0005$), and GI-specific anxiety symptoms ($P = .06$) were associated with somatization levels ($R^2 = 0.35$). Levels of general and GI-specific anxiety and depressive symptoms partially mediated this physical coping effect. The effect of psychological coping resources (including optimism, social support, and accepting/expressing emotions) on somatization levels was not significant ($P = .98$), but was fully mediated by levels of anxiety and depressive symptoms, and partially by levels of GI-specific anxiety symptoms.

CONCLUSIONS: In a cross-sectional study of patients with IBS in Sweden, we found associations of levels of coping resources with GI and extraintestinal symptom severity; these associations were mediated by levels of anxiety and depressive symptoms. Although confirmation in longitudinal studies is needed, this identifies coping as a potential psychological treatment target in IBS.

Keywords: Functional Disorders; Coping Resources; Anxiety; Depression; Somatization.

See editorial on page 1500.

Neither the etiology of irritable bowel syndrome (IBS) nor its pathophysiology are fully understood, but it is generally accepted that dysfunction of brain-gut signaling plays a key role.¹ Peripheral factors, including immunologic, microbiologic, and neuroendocrine, affect afferent signals conveyed along the brain-gut axis,² which in turn are centrally modulated by

psychological processes, such as attention toward and fear of bodily/gastrointestinal (GI) symptoms, and

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Abbreviations used in this paper: CRI, Coping Resources Inventory; FD, functional dyspepsia; GI, gastrointestinal; IBS, irritable bowel syndrome.

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1542-3565/\$36.00

<http://dx.doi.org/10.1016/j.cgh.2017.02.032>

psychiatric comorbidity, such as depressive and anxiety disorders.¹ The brain-gut axis therefore provides the necessary biologic framework to support a biopsychosocial conceptualization of IBS. More specifically, these psychobiologic processes may underlie the relationship between psychological processes or states and reporting of (medically unexplained) GI or, more broadly, somatic symptoms.³

Within this biopsychosocial conceptualization, the previously mentioned psychological processes have been studied extensively, whereas others, including coping resources, have received relatively little attention.³ Coping can be defined as a process consisting of action-oriented and intrapsychic efforts to manage the demands created by stressful events.^{4,5} Coping resources, including relatively stable individual differences in optimism, social support, acceptance and expression of emotions (psychological coping resources), and the tendency to practice activities that are beneficial for health, including physical exercise and eating healthy foods (physical coping resources) can aid in this process, and in turn affect coping processes. Coping efforts can be adaptive or maladaptive (ie, result in successful resolution of a stressor or not, and coping resources and processes have been shown to affect both physical and mental health.^{4,6} Altered levels of coping resources have been reported in IBS and other functional GI disorders compared with healthy or organic disease control populations.⁷⁻¹¹ However, these studies were case-control studies, and few studies have evaluated the relationship between levels of coping resources on the one hand and levels of GI and extraintestinal somatic symptoms on the other, taking the levels of psychological symptoms into account.¹²

Multiple (medically unexplained) extraintestinal somatic symptoms, such as headache, musculoskeletal pain, and urinary symptoms, are frequent in IBS,¹³ and the collective severity of these symptoms is often quantified and referred to as "somatization."^{14,15} An association between levels of somatization, GI symptoms, self-ratings of health, and number of health care visits has been demonstrated in IBS,^{16,17} and the type of comorbid somatic symptoms is associated with distress and reduction of quality of life.¹⁸ Moreover, comorbidity with anxiety disorders and depression among patients with IBS is high.¹⁹ Furthermore, levels of symptom-specific anxiety have been shown to be associated with higher somatic symptom severity in chronic pain disorders in general,²⁰ and in patients with IBS specifically.²¹

Thus, altered levels of coping resources, and increased levels of anxiety and depressive symptoms, and extraintestinal somatic symptoms (ie, somatization), have all been described in IBS, but the relationship between these features remains understudied. We therefore aimed to study the association between levels of coping resources on the one hand, and GI symptoms and somatization on the other, in IBS. Somatization was used as an outcome in addition to GI symptom severity to elucidate whether the relationships found are specific to the core GI symptoms

of IBS, or generalize to somatic symptom reporting in general. We hypothesized an association between levels of coping resources and levels of both somatic symptom reporting in general (somatization) and GI symptoms more specifically, because coping resources have been linked to a wide variety of physical health outcomes rather than specific ones.⁴ We also hypothesized that these putative associations would be mediated by levels of depressive and (GI symptom-specific) anxiety symptoms, based on longitudinal evidence demonstrating that lower levels of coping resources may lead to increased levels of anxiety and depression symptoms,^{22,23} which are in turn associated with IBS diagnosis and somatization.²⁴ Furthermore, levels of coping resources are considered to be relatively stable over time ("trait" characteristics), contrary to levels of anxiety and depressive symptoms ("state" characteristics).^{4,6}

Materials and Methods

Study Population and Data Collection

Patients aged 18–70 years fulfilling the ROME II criteria²⁵ for IBS were recruited from 2 studies with the main objective to investigate pathophysiology and symptoms.^{26,27} The patients were included between 2003 and 2007 at a secondary/tertiary care outpatient center specialized in functional GI disorders.

Self-Assessment Questionnaires

The patients completed the following validated self-assessment questionnaires in privacy on site at their first study visit to assess coping resources, psychological and GI symptoms, and somatization: Coping Resources Inventory (CRI),⁶ Gastrointestinal Symptom Rating Scale,²⁸ Hospital Anxiety and Depression Scale,²⁹ Visceral Sensitivity Index,³⁰ and Symptom Check List-90 Revised.³¹ In this study we only used the somatization subscale of Symptom Check List-90 Revised. For detailed descriptions of these questionnaires, see the [Supplementary Material](#).

Statistical Methods

Details of statistical methods are provided in the [Supplementary Material](#). Briefly, the number of subscales of the CRI was first reduced using factor analysis. The resulting factor scores were associated with GI symptom severity and somatization using bivariate Pearson correlations and 2 stepwise General Linear Model analyses (step 1, coping resources; step 2, general and symptom-specific anxiety, depression), 1 for each of the outcomes (GI symptom severity, somatization). Putative mediation of the effect of coping resources on GI symptom severity and somatization by psychological state variables was tested using the Baron and Kenny method.

Results

Subjects

We included 250 patients with IBS and after exclusions caused by incomplete completion of questionnaires, 216 patients with IBS remained for the analyses in this study. There were no significant differences in gender (distribution prior/post exclusion: 177/151 female and 73/65 male) or age (mean age prior/post exclusion: 40.0/40.4 years) distribution after exclusions. For more extensive information on the study population, see the [Supplementary Material](#). Descriptive results of the 5 subscales of CRI, Hospital Anxiety and Depression Scale, Visceral Sensitivity Index, and Gastrointestinal Symptom Rating Scale, including the proportion of subjects with clinically significant anxiety and depression using validated cutoff levels,²⁹ are displayed in [Supplementary Table 1](#).

Factor Analysis

In a factor analysis on the 5 CRI subscales scores, 3 factors were retained, jointly explaining 88% of the variance ([Table 1](#)). The interpretation of the resulting factors was straightforward. Factor 1 was termed “psychological coping” because the cognitive, social, and emotional CRI subscales showed high loadings on this factor. Factor 2 “spiritual coping” and Factor 3 “physical coping” were both characterized by high loadings of the single respective CRI subscales only. Cross-loadings were low (all < 0.33).

Bivariate Associations

Better physical coping was associated with lower levels of GI symptom severity ($r = -0.31$; $P < .0001$), whereas lower levels of both psychological ($r = -0.24$; $P = .0004$) and physical coping resources ($r = -0.34$; $P < .0001$) were associated with more severe somatization ([Table 2](#)). More severe general anxiety was associated with lower levels of psychological ($r = -0.32$; $P < .0001$), spiritual ($r = -0.23$; $P = .0001$), and physical coping

Table 1. Results of Factor Analysis of CRI: Rotated Factor Pattern

Coping, subscale	Factor 1: psychological coping	Factor 2: spiritual coping	Factor 3: physical coping
Cognitive	0.75	0.32	0.31
Social	0.91	0.15	0.09
Emotional	0.87	0.23	0.13
Spiritual	0.29	0.95	0.05
Physical	0.18	0.05	0.98

NOTE. The numbers in the table are factor loadings.

Table 2. Bivariate Associations: Coping Factors, Somatization, GI, and Psychological Symptoms

	Factor 1: psychological coping	Factor 2: spiritual coping	Factor 3: physical coping
GI symptoms (GSRS)	-0.02	-0.05	-0.31 ^a
Somatization (SCL-90R)	-0.24 ^a	0.01	-0.34 ^a
Anxiety (HADS)	-0.32 ^a	-0.23 ^a	-0.19 ^b
Depression (HADS)	-0.53 ^a	-0.09	-0.25 ^a
GI-specific anxiety (VSI)	-0.22 ^b	-0.11	-0.20 ^b

Pearson correlation coefficients: ^a $P < .001$, ^b $P < .01$. GSRS, Gastrointestinal Symptom Rating Scale; HADS, Hospital Anxiety and Depression Scale; SCL-90R, Symptom Check List-90 Revised; VSI, Visceral Sensitivity Index.

($r = -0.19$; $P = .007$). More severe depression and GI-specific anxiety were associated with lower levels of psychological ($r = -0.53$, $P < .0001$; and $r = -0.22$, $P = .002$, respectively) and physical coping resources ($r = -0.26$, $P = .0002$; and $r = -0.20$, $P = .005$, respectively) ([Table 2](#)).

General Linear Models and Mediation Analyses

Outcome 1: gastrointestinal symptom severity (Gastrointestinal Symptom Rating Scale)

First step: Level of physical coping resources was significantly associated with GI symptom severity ([Table 3](#)).

Second step: When adding levels of general and GI-specific anxiety, and depressive symptoms as covariates to the model, indication of (partial) mediation was found, because the significance of the relationship between level of physical coping resources and GI symptom severity was reduced ([Table 3](#)). The effects of level of physical coping resources, and of general and GI-specific anxiety symptoms, were significant, whereas the effect of level depressive symptoms was not. The variables in the model jointly explained 31% of the variance in GI symptom severity.

Mediation analyses: The effect of level of physical coping resources on GI symptom severity was partially

Table 3. GLMs for GI Symptom Severity

	$\beta \pm SE$	F_{variable}	P_{variable}
GLM step 1 ^a			
Physical coping	-0.26 ± 0.1	22.08	< .0001
GLM step 2 ^b			
Physical coping	-0.17 ± 0.05	10.31	.0016
Anxiety	0.033 ± 0.015	4.63	.0327
Depression	0.003 ± 0.018	0.02	.89
GI-specific anxiety	0.018 ± 0.004	24.45	< .0001

GLM, General Linear Model.

^aModel: $F_{1,206} = 22.08$; $P < .0001$; $R^2 = 0.10$.

^bModel: $F_{4,190} = 21.14$; $P < .0001$; $R^2 = 0.31$.

mediated by levels of general (Sobel test: $z = 2.39$; $P = .017$) and GI-specific anxiety ($z = 2.64$; $P = .008$) symptoms (details for GI-specific anxiety in Figure 1A, details not shown for general anxiety). When the position of the independent (coping) and mediator (anxiety) variables were flipped, level of physical coping resources was found to partially mediate the effects of both levels of general ($z = 2.23$; $P = .026$) and GI-specific anxiety ($z = 2.21$; $P = .027$) symptoms on GI symptom severity, thereby providing evidence for the alternative path with level of physical coping resources as the mediator rather than independent variable.

Outcome 2: somatization (Symptom Check List-90 Revised)

First step: Levels of physical and psychological coping resources were independently associated with somatization (Table 4).

Second step: When adding levels of anxiety (general and GI-specific) and depressive symptoms as covariates to the General Linear Model, the effect of level of psychological coping resources became nonsignificant and

also the strength of the effect of level of physical coping resources was reduced, although still significant, giving an indication of full and partial mediation, respectively. The effects of levels of physical coping resources, and of general anxiety and depression symptoms, were significant, whereas the effect of level of GI-specific anxiety symptoms showed a trend ($P = .06$). The variables in the model jointly explained 35% of the variance in somatization levels (Table 4).

Mediation analyses: The effect of level of psychological coping resources on somatization was fully mediated by levels of anxiety (Sobel test: $z = 3.78$; $P = .0001$) and depressive ($z = 5.63$; $P < .0001$) symptoms, and partially mediated by levels of GI-specific anxiety symptoms ($z = 2.73$; $P = .006$) levels (details for level of depressive symptoms shown in Figure 1B).

The effect of level of physical coping resources on somatization was partially mediated by levels of anxiety (Sobel test: $z = 2.50$; $P = .012$), depressive ($z = 3.33$; $P = .0008$), and GI-specific anxiety ($z = 2.48$; $P = .013$)

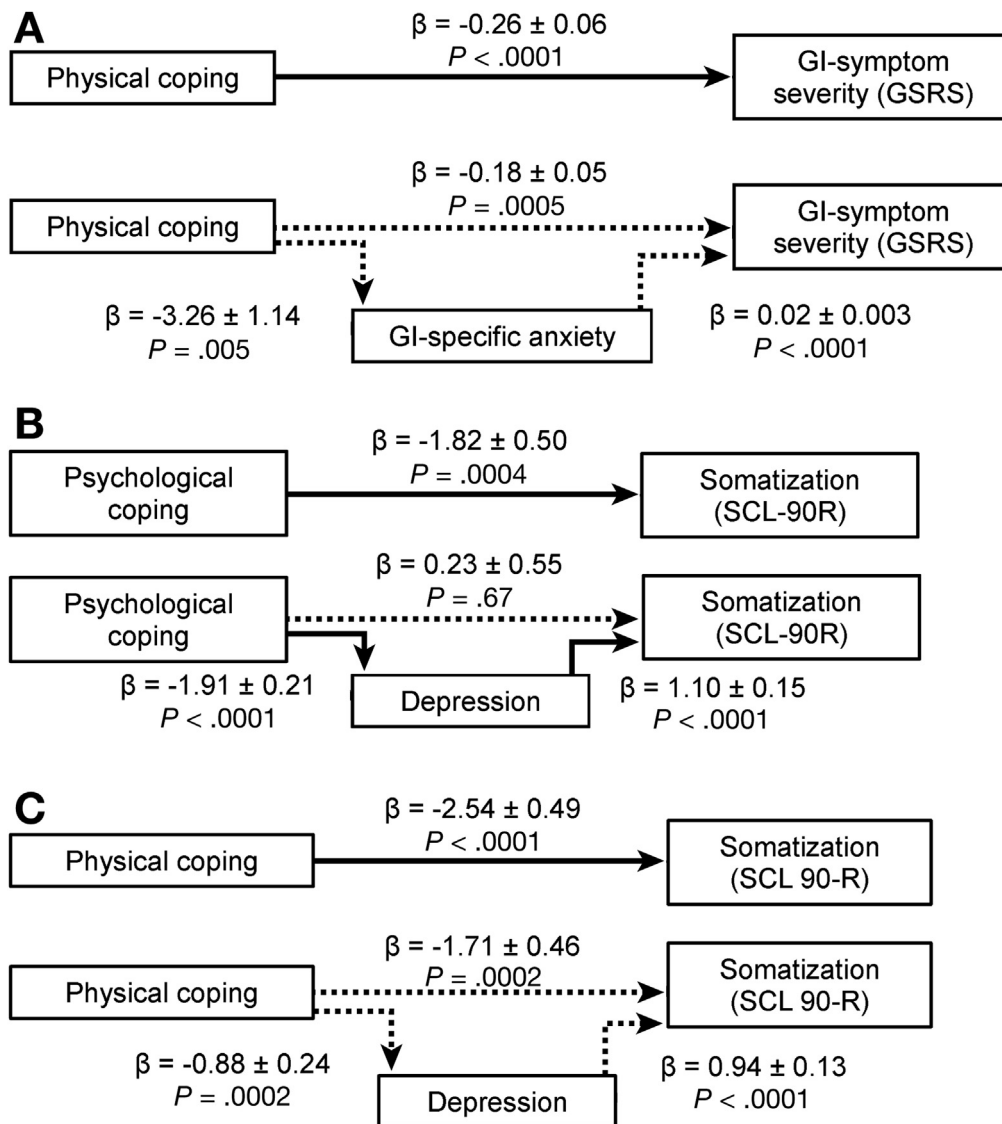


Figure 1. Mediation analyses where it is demonstrated that (A) the association between physical coping and GI symptom severity is partially mediated by GI-specific anxiety (Sobel test for significance of indirect effect: $z = 2.64$; $P = .008$), (B) the association between psychological coping and somatization is fully mediated by depression (Sobel test for significance of indirect effect: $z = 5.63$; $P < .0001$), and (C) the association between physical coping and somatization is partially mediated by depression (Sobel test for significance of indirect effect: $z = 3.33$; $P = .0008$). GSRs, Gastrointestinal Symptom Rating Scale; SCL-90R, Symptom Check List-90 Revised.

Table 4. GLMs for Somatization

	$\beta \pm SE$	$F_{variable}$	$P_{variable}$
GLM step 1^a			
Psychological coping	-1.8 ± 0.5	14.76	.0002
Physical coping	-2.53 ± 0.5	28.75	< .0001
GLM step 2^b			
Psychological coping	0.014 ± 0.55	0.00	.98
Physical coping	-1.40 ± 0.47	9.04	.003
Anxiety	0.33 ± 0.13	6.06	.0147
Depression	0.64 ± 0.18	12.44	.0005
GI-specific anxiety	0.06 ± 0.03	3.57	.0604

GLM, General Linear Model.

^aModel: $F_{2,210} = 21.80$; $P < .0001$; $R^2 = 0.17$.

^bModel $F_{5,188} = 19.90$; $P < .0001$; $R^2 = 0.35$.

symptoms (details for level of depressive symptoms in Figure 1C). For further information on mediation analyses, see the [Supplementary Material](#).

Discussion

We demonstrated that lower levels of physical and psychological coping resources are associated with increased GI and extraintestinal somatic symptom severity in IBS, and that these associations are (partially) mediated by levels of anxiety and depressive symptoms. However, evidence was also found for the alternative path in which level of physical coping resources partially mediates the effect of levels of anxiety and depressive symptoms on GI symptom severity and somatization; this was not the case for level of psychological coping resources.

In IBS, both physiological and psychosocial factors are believed to contribute to the occurrence and severity of GI symptoms.³² Several studies have explored the connection between psychosocial factors and IBS, but research on the role of coping resources specifically is sparse, and almost exclusively limited to what we in the results refer to as psychological coping resources, consisting of the cognitive, social, and emotional subscales of the CRI. Specifically, patients with IBS have been found to use a more emotionally focused coping style,¹⁰ and to use positive reappraisal less frequently compared with patients with organic GI diseases.³³ Abnormalities in coping style (more specifically, an inflexible, action-oriented coping style, such as problem-solving and confrontation) have been reported in patients with functional dyspepsia (FD).^{34,35} It has also been shown that maladaptive psychological coping strategies (specifically, catastrophizing and decreased self-perceived ability to decrease symptoms) are predictors for various indicators of poor health outcome in both functional and organic GI disorders.³³ Catastrophizing represents a maladaptive cognitive coping process that is frequently present among patients with IBS.¹¹ Catastrophizing is defined as “a negative cognitive process of

exaggerated negative rumination and worry,”³⁶ which in our study was best represented by the (inverse of) the cognitive subscale of the CRI. Moreover, higher levels of catastrophizing are associated with more severe pain in IBS.¹¹ In line with these findings, our study has demonstrated that lower levels of psychological coping resources, including the cognitive domain, were associated with higher levels of somatization (ie, levels of painful extraintestinal symptoms).

Furthermore, we demonstrated that level of physical coping resources in patients with IBS was independently associated with GI symptom severity, and with somatization. The association between level of physical coping resources and GI symptom severity is of interest, because a recent study from our group highlighted the benefit of physical activity for IBS symptoms,³⁷ with physical activity being an important component of physical coping resources. Moreover, there is growing evidence that adopting a “healthier” diet, another important component of physical coping resources, even without specifically restricting certain nutrients, improves IBS symptoms.³⁸ To the best of our knowledge, the specific effects of physical coping resources have not been studied before in IBS.

Moreover, the existing studies where impaired levels of (psychological) coping resources in IBS have been documented and linked to health outcomes have evaluated coping as a separate factor, without taking interaction with other potentially relevant factors into account.^{33,39} Although the frequent presence of anxiety and depressive symptoms in IBS is well known,^{40,41} the role of levels of anxiety and depressive symptoms in the association between coping strategies and symptoms in IBS has not previously been investigated. In FD, however, it has been shown that anxiety and depression are associated with impaired coping.^{34,35,42}

The effect of level of physical coping on both GI symptom severity and somatization was partially mediated by levels of anxiety and depressive symptoms. This is in line with a large body of evidence showing that physical exercise and dietary interventions (which constitute important components of physical coping resources) can reduce levels of anxiety and depressive symptoms.^{43,44} However, we also found evidence for an alternative path in which level of physical coping resources acts as the mediator of the psychological-somatic symptom relationship. It is indeed conceivable that physical coping resources are less stable over time compared with psychological coping resources, and there is evidence that depressive episodes are associated with a less healthy lifestyle, both in terms of physical exercise and diet.⁴⁵ Moreover, level of psychological coping resources was, independent of physical coping, associated with somatization, but this effect was fully mediated by levels of depressive and general anxiety symptoms. No evidence for an alternative path model with level of coping resources as the mediator was found here, which is in line with the conceptualization of

(psychological) coping resources as a stable trait predisposing to various negative psychological and somatic health outcomes.⁴

Although sufficient caution is warranted, because our findings need to be confirmed in longitudinal studies, they may have implications toward IBS treatment. Because coping is not an innate capacity, but can change over time,⁵ strengthening coping resources could potentially improve symptoms in patients with IBS. Previous research in FD may serve as an example here. The finding of a nondiscriminative, inflexible coping style,^{34,35} defined as “the ability to discontinue an ineffective coping strategy and produce and implement an alternative coping strategy,”⁴⁶ led to the development of a specific intervention to improve coping flexibility. It was shown that such “flexible coping psychotherapy” not only improved coping flexibility, but also FD symptoms, and that the improvement on both these parameters correlated.

This study has several limitations that should be addressed. First, mediation in the strict sense requires temporal precedence of the mediator by the mediated variable.^{47,48} Because this study is cross-sectional, we do not have temporal precedence, and the order of variables in the regression model is therefore based on theoretical and empirical grounds from the existing literature rendering this chronological order plausible.^{22–24} The cross-sectional design restricts from conclusions being drawn regarding the temporal order of events and, hence, regarding causality. Confirmation of these results in longitudinal studies is therefore needed, especially regarding the results on physical coping resources, because we found evidence supporting an alternative path model in which level of physical coping resources mediates the effect of levels of anxiety and depressive symptoms on somatic symptom severity. Furthermore, because this study did not include any control group, we cannot conclude whether these findings are specific to patients with IBS or equally apply to other patient groups characterized by (medically unexplained) GI and/or extraintestinal symptoms, and our findings from a secondary/tertiary care IBS population cannot be generalized to a primary care population. Finally, we only tested a limited number of potentially relevant mediators; hence, additional ones may need to be taken into account in future studies (eg, symptom-specific psychological processes such as health-related or pain-specific anxiety).

Despite these limitations, our results identify coping resources as a relevant factor associated with GI and extraintestinal symptom severity in IBS. Both components of the mediational pathway, impaired coping and anxiety and depression levels, may thus serve as potential targets for improving somatic symptoms in IBS. However, the effect of physical coping is only partially mediated through psychological symptom levels; therefore, it may be useful to target both physical coping mechanisms and psychological symptoms to improve somatic symptom severity in IBS.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at <http://dx.doi.org/10.1016/j.cgh.2017.02.032>.

References

1. Fichna J, Storr MA. Brain-gut interactions in IBS. *Front Pharmacol* 2012;3:127.
2. Camilleri M, Di Lorenzo C. Brain-gut axis: from basic understanding to treatment of IBS and related disorders. *J Pediatr Gastroenterol Nutr* 2012;54:446–453.
3. Van Oudenhove L, Levy RL, Crowell MD, et al. Biopsychosocial aspects of functional gastrointestinal disorders. *Gastroenterology* 2016;150:1355–1367.
4. Taylor SE, Stanton AL. Coping resources, coping processes, and mental health. *Annu Rev Clin Psychol* 2007;3:377–401.
5. Lazarus RS, Folkman S. Stress, appraisal, and coping. New York: Springer, 1984:141–327.
6. Hammer ALM. Coping Resources Inventory manual. Palo Alto, CA: Consulting Psychologist Press, 1988.
7. Pellissier S, Dantzer C, Canini F, et al. Psychological adjustment and autonomic disturbances in inflammatory bowel diseases and irritable bowel syndrome. *Psychoneuroendocrinology* 2010; 35:653–662.
8. Jones MP, Wessinger S, Crowell MD. Coping strategies and interpersonal support in patients with irritable bowel syndrome and inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2006;4:474–481.
9. De la Roca-Chiapas JM, Solis-Ortiz S, Fajardo-Araujo M, et al. Stress profile, coping style, anxiety, depression, and gastric emptying as predictors of functional dyspepsia: a case-control study. *J Psychosom Res* 2010;68:73–81.
10. Wrzesinska MA, Kocur J. [The assessment of personality traits and coping style level among the patients with functional dyspepsia and irritable bowel syndrome]. *Psychiatr Pol* 2008; 42:709–717.
11. Surdea-Blaga T, Baban A, Dumitrascu DL. Psychosocial determinants of irritable bowel syndrome. *World J Gastroenterol* 2012;18:616–626.
12. Phillips K, Wright BJ, Kent S. Psychosocial predictors of irritable bowel syndrome diagnosis and symptom severity. *J Psychosom Res* 2013;75:467–474.
13. Enck P, Aziz Q, Barbara G, et al. Irritable bowel syndrome. *Nat Rev Dis Primers* 2016;2:16014.
14. Whitehead WE. Psychosocial aspects of functional gastrointestinal disorders. *Gastroenterol Clin North Am* 1996;25:21–34.
15. Lipowski ZJ. Somatization: the concept and its clinical application. *Am J Psychiatry* 1988;145:1358–1368.
16. Drossman DA, Li Z, Andruzzi E, et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, socio-demography, and health impact. *Dig Dis Sci* 1993; 38:1569–1580.
17. Lackner JM, Gudleski GD, Thakur ER, et al. The impact of physical complaints, social environment, and psychological functioning on IBS patients' health perceptions: looking beyond GI symptom severity. *Am J Gastroenterol* 2014; 109:224–233.
18. Lackner JM, Ma CX, Keefer L, et al. Type, rather than number, of mental and physical comorbidities increases the severity of

- symptoms in patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol* 2013;11:1147–1157.
19. Mayer EA, Craske M, Naliboff BD. Depression, anxiety, and the gastrointestinal system. *J Clin Psychiatry* 2001;62 Suppl 8:28–36; discussion 37.
 20. Asmundson GJ, Norton PJ, Norton GR. Beyond pain: the role of fear and avoidance in chronicity. *Clin Psychol Rev* 1999;19:97–119.
 21. Jerndal P, Ringstrom G, Agerforz P, et al. Gastrointestinal-specific anxiety: an important factor for severity of GI symptoms and quality of life in IBS. *Neurogastroenterol Motil* 2010;22:646.
 22. Morris MC, Kouros CD, Fox KR, et al. Interactive models of depression vulnerability: the role of childhood trauma, dysfunctional attitudes, and coping. *Br J Clin Psychol* 2014; 53:245–263.
 23. Chan CS, Rhodes JE. Religious coping, posttraumatic stress, psychological distress, and posttraumatic growth among female survivors four years after Hurricane Katrina. *J Trauma Stress* 2013;26:257–265.
 24. Koloski NA, Jones M, Kalantar J, et al. The brain–gut pathway in functional gastrointestinal disorders is bidirectional: a 12-year prospective population-based study. *Gut* 2012;61:1284–1290.
 25. Drossman DA. Rome II: the functional gastrointestinal disorders: diagnosis, pathophysiology, and treatment: a multinational consensus. McLean, VA: Degnon Associates, 2000.
 26. Posserud I, Syrös A, Lindstrom L, et al. Altered rectal perception in irritable bowel syndrome is associated with symptom severity. *Gastroenterology* 2007;133:1113–1123.
 27. Tornblom H, Van Oudenhove L, Sadik R, et al. Colonic transit time and IBS symptoms: what's the link? *Am J Gastroenterol* 2012;107:754–760.
 28. Dimenas E, Glise H, Hallerback B, et al. Well-being and gastrointestinal symptoms among patients referred to endoscopy owing to suspected duodenal ulcer. *Scand J Gastroenterol* 1995;30:1046–1052.
 29. Zigmund AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–370.
 30. Labus JS, Bolus R, Chang L, et al. The Visceral Sensitivity Index: development and validation of a gastrointestinal symptom-specific anxiety scale. *Aliment Pharmacol Ther* 2004;20:89–97.
 31. Craighead WE, Nemeroff CB. NetLibrary Inc. The Corsini encyclopedia of psychology and behavioral science. Volume 1–4. 3rd ed. New York: Wiley 2001.
 32. Drossman DA. Presidential address: gastrointestinal illness and the biopsychosocial model. *Psychosom Med* 1998;60:258–267.
 33. Drossman DA, Leserman J, Li Z, et al. Effects of coping on health outcome among women with gastrointestinal disorders. *Psychosom Med* 2000;62:309–317.
 34. Cheng C, Hui WM, Lam SK. Coping style of individuals with functional dyspepsia. *Psychosom Med* 1999;61:789–795.
 35. Cheng C, Hui W, Lam S. Perceptual style and behavioral pattern of individuals with functional gastrointestinal disorders. *Health Psychol* 2000;19:146–154.
 36. Keogh E. Negative affectivity, catastrophizing and anxiety sensitivity. In: Asmundson GJG, Crombez G, eds. *Understanding and treating fear of pain*. New York: Oxford University Press, 2004:91–117.
 37. Johannesson E, Simren M, Strid H, et al. Physical activity improves symptoms in irritable bowel syndrome: a randomized controlled trial. *Am J Gastroenterol* 2011;106:915–922.
 38. Bohn L, Storsrud S, Liljebo T, et al. Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. *Gastroenterology* 2015;149:1399–1407 e2.
 39. Drossman DA, Whitehead WE, Toner BB, et al. What determines severity among patients with painful functional bowel disorders? *Am J Gastroenterol* 2000;95:974–980.
 40. Harter MC, Conway KP, Merikangas KR. Associations between anxiety disorders and physical illness. *Eur Arch Psychiatry Clin Neurosci* 2003;253:313–320.
 41. Folks DG, Kinney FC. The role of psychological factors in gastrointestinal conditions. A review pertinent to DSM-IV. *Psychosomatics* 1992;33:257–270.
 42. Cheng C, Hui WM, Lam SK. Psychosocial factors and perceived severity of functional dyspeptic symptoms: a psychosocial interactionist model. *Psychosom Med* 2004; 66:85–91.
 43. Quirk SE, Williams LJ, O'Neil A, et al. The association between diet quality, dietary patterns and depression in adults: a systematic review. *BMC Psychiatry* 2013;13:175.
 44. Wegner M, Helmich I, Machado S, et al. Effects of exercise on anxiety and depression disorders: review of meta-analyses and neurobiological mechanisms. *CNS Neurol Disord Drug Targets* 2014;13:1002–1014.
 45. Lopresti AL, Hood SD, Drummond PD. A review of lifestyle factors that contribute to important pathways associated with major depression: diet, sleep and exercise. *J Affect Disord* 2013; 148:12–27.
 46. Kato T. Development of the Coping Flexibility Scale: evidence for the coping flexibility hypothesis. *J Couns Psychol* 2012;59:262–273.
 47. Kraemer HC, Stice E, Kazdin A, et al. How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *Am J Psychiatry* 2001; 158:848–856.
 48. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986; 51:1173–1182.

Reprint requests

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Conflicts of interest

These authors disclose the following: Hans Tornblom has served as Consultant/Advisory Board member for Almirall, Danone, and Shire. Jan Tack has given scientific advice to Almirall, AstraZeneca, Danone, Menarini, Novartis, Nycomed, Ocera, Ono pharma, Shire, SK Life Sciences, Theravance, Tranzyme, Xenoport, and Zeria Pharmaceuticals; and has been member of the Speaker bureau for Abbott, Almirall, AlfaWasserman, AstraZeneca, Janssen, Menarini, Novartis, Nycomed, Shire, and Zeria. Magnus Simrén has received unrestricted research grants from Danone and Ferring Pharmaceuticals; served as a Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albireo, Glycom, and Shire; and as a speaker for Tillotts, Takeda, Shire, and Almirall. Lukas Van Oudenhove is assistant research professor of the KU Leuven Special Research Fund (Bijzonder Onderzoeksfonds, BOF). The remaining authors disclose no conflicts.

Funding

This study was supported by the Swedish Medical Research Council (grants 13409, 21691, and 21692); the Marianne and Marcus Wallenberg Foundation; AFA Försäkring; University of Gothenburg; Centre for Person-Centered Care, Sahlgrenska Academy, University of Gothenburg; and by the Faculty of Medicine, University of Gothenburg.

Supplementary Materials and Methods

Study Population and Data Collection

Most patients were referred from primary care, and a smaller proportion through self-referral or from gastroenterologists, and the diagnosis was based on a typical clinical presentation and additional investigations if considered necessary by the gastroenterologist (M.S.). Exclusion criteria were other GI diseases explaining the symptoms; severe diseases, such as malignancy, heart disease, kidney disease, or neurologic disease; severe psychiatric disease; or pregnancy. The studies were approved by the Regional Ethical Review Board in Gothenburg, Sweden. Each participant was verbally informed about the study and was given written information, before giving written informed consent to participate in the studies.

Self-Assessment Questionnaires

- CRI¹: One of the goals in developing the CRI was to provide a tool for identifying resources currently available to individuals for managing stress. Clinical theory and practice largely focus on what is wrong with people rather than on what is right with them. The CRI was constructed to facilitate an emphasis on resources rather than deficits.¹ The CRI consists of 60 statements, subdivided into 5 domains. The statements are answered on an ordinal scale (1–4), ranging from never or seldom to almost always or always. A score for each domain and a total CRI score can be calculated by summing up the respective items. The different domains reflect the ability of an individual to respond to, handle, and recover from stressful situations.
 - Cognitive: how generally optimistic the individual is, and to what extent the person keeps a positive outlook on oneself and toward others. Example statement: “I feel as valuable as anyone else.”
 - Social: to what extent the person belongs to a social context that is supportive in stressful situations. “I am part of a group, other than my family that cares about me.”
 - Emotional: to what extent the person can accept and express a variety of emotions, based on a principle that the long-term negative effects of stress can be soothed with the help of emotional responses. “I can cry when I am sad.”
 - Spiritual: to what extent the actions of the individual are driven by personal convictions or religious, familial, or cultural traditions. These traditions may aid in stressful situations by giving them a purpose and provide ways of effective responses. “I know what is important in life.”
 - Physical: to what extent the person exercises and takes part in activities that promote physical health. It is believed that a high level of physical well-being decreases negative stress reactions and aids in a faster recovery. “I exercise vigorously 3 to 4 times a week.”¹
- Hospital Anxiety and Depression Scale²: Assesses the presence and severity of anxiety and depression symptoms during the past week by 7 questions on each domain, and is specifically designed to be used in nonpsychiatric settings. Each response is scored 0–3, with 3 indicating the most severe symptom level. The scores for anxiety and depression are calculated separately and each have a range of 0–21.²
- Visceral Sensitivity Index³: A widely used and well-validated measurement of anticipatory anxiety concerning the likely occurrence of GI symptoms.^{3–5} Five dimensions of GI symptom-specific anxiety (worry, fear, sensitivity, attentiveness, and avoidance) are investigated through 15 statements that are assessed through a 6-point Likert scale, ranging from strongly agree to strongly disagree. The scores range from 0 to 75, with a higher score indicating more severe the GI symptom-specific anxiety.^{3,5}
- Gastrointestinal Symptom Rating Scale⁶: A reliable instrument to assess distinct groups of GI symptoms: reflux, indigestion, abdominal pain, constipation, and diarrhea. The questionnaire consists of 15 items, which are scored on a 7-point Likert scale, ranging from no symptoms (=1) to very severe symptoms (=7). A higher score indicates more severe symptoms.
- Symptom Check List-90 Revised⁷: Evaluates a wide variety of psychological symptoms and distress. The questionnaire covers 9 symptom dimensions (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) through 90 statements. Each statement is scored on a 5-point scale, ranging from no symptoms (=0) to extreme symptoms (=4). A higher score indicates more severe symptoms in that dimension. The dimensions can also be added into 3 different global distress indices. In this study we only used the somatization subscale. Somatization refers to the tendency to experience and express psychological distress as somatic symptoms and seek medical assistance for the symptoms.

Statistical Methods

All analyses were done using SAS 9.1 software (SAS Institute, Cary, NC). Data are presented as mean ± standard deviation; significance level was set at $P < .05$ (2-tailed). The number of subscales of the CRI was first reduced through factor analysis on the 5 subscale scores (principal components method, orthogonal varimax

rotation), thereby also orthogonalizing the resulting factors to avoid multicollinearity when using them as independent variables in subsequent General Linear Model (GLM) analyses (see below). The criterion to retain a factor was explained proportion of the variance > 10%. Bivariate associations were explored between the retained coping resources factors on the one hand, and levels of GI symptoms, somatization, and (GI-specific and general) anxiety and depression symptoms on the other, using Pearson correlations.

Coping resources factors significantly associated with GI symptom severity or somatization in bivariate correlation analyses were further analyzed in 2 GLMs. The coping resources factors were first entered as independent variables in the respective GLM with GI symptom severity and somatization as the dependent variables. Secondly, levels of depressive, general and GI-specific anxiety symptoms were added as covariates.

Traditionally mediation requires temporal precedence of the mediator by the independent variable^{8,9}; mediation was thus used in a more restricted sense in this cross-sectional study. However, the order in which the variables were entered in the GLM was chosen according to a plausible chronological order based on theoretical and empirical grounds, as outlined in the introduction. Furthermore, we tested alternative paths by flipping the position of the independent and mediator variables (ie, testing whether the effect of levels of anxiety and depressive symptoms on levels of GI symptoms and somatization is mediated by levels of coping resources).

The potential mediation effects of levels of general anxiety, depressive, and GI-specific anxiety symptoms on the coping resources (GI symptom severity and somatization relationship) were tested using the Baron and Kenny method, with the Sobel test for the significance of the indirect effect.⁹ When investigating mediation, it is required that the potential mediator is associated with the independent variable, and that it significantly reduces the strength of the effect of this independent variable on the dependent variable when added to the model.⁸

Results: Somatization (Symptom Check List-90 Revised) Mediation analyses

Psychological Coping Resources: Effect on Somatization

The effect of level of physical coping resources on somatization was partially mediated by levels of anxiety (Sobel test: $z = 2.50$; $P = .012$), depressive ($z = 3.33$; $P = .0008$), and GI-specific anxiety ($z = 2.48$; $P = .013$)

symptoms (details for level of depressive symptoms in Figure 1C).

When the position of the independent (coping) and mediator (anxiety, depressive symptoms) variables were flipped, no evidence for mediation was found (effect of the mediator nonsignificant, strength of effect of the independent variable not reduced), arguing against the alternative path with level of psychological coping resources as the mediator rather than the independent variable.

Physical Coping Resources: Effect on Somatization

When the position of the independent (coping) and mediator (anxiety, depression) variables were flipped, level of physical coping resources was found to partially mediate the effects of levels of general anxiety ($z = 2.30$; $P = .021$), depressive ($z = 2.65$; $P = .008$), and GI-specific anxiety symptom levels ($z = 2.30$; $P = .022$) on somatization, thereby providing evidence for the alternative path with level of physical coping resources as the mediator rather than the independent variable.

References

1. Hammer ALM. Coping Resources Inventory manual. Paolo Alto, CA: Consulting Psychologist Press, 1988.
2. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;67:361–370.
3. Labus JS, Bolus R, Chang L, et al. The Visceral Sensitivity Index: development and validation of a gastrointestinal symptom-specific anxiety scale. *Aliment Pharmacol Ther* 2004;20:89–97.
4. Labus JS, Mayer EA, Chang L, et al. The central role of gastrointestinal-specific anxiety in irritable bowel syndrome: further validation of the Visceral Sensitivity Index. *Psychosom Med* 2007;69:89–98.
5. Jerndal P, Ringstrom G, Agerforz P, et al. Gastrointestinal-specific anxiety: an important factor for severity of GI symptoms and quality of life in IBS. *Neurogastroenterol Motil* 2010;22:646.
6. Dimenas E, Glise H, Hallerback B, et al. Well-being and gastrointestinal symptoms among patients referred to endoscopy owing to suspected duodenal ulcer. *Scand J Gastroenterol* 1995;30:1046–1052.
7. Craighead WE, Nemeroff CB. NetLibrary Inc. The Corsini encyclopedia of psychology and behavioral science. Volume 1–4. 3rd ed. New York: Wiley 2001.
8. Kraemer HC, Stice E, Kazdin A, et al. How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *Am J Psychiatry* 2001; 158:848–856.
9. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986; 51:1173–1182.

Supplementary Table 1. Results From Questionnaires in Patients With IBS Measuring Coping Resources, Anxiety (General and GI-Specific), Depression, and GI and Extraintestinal Symptoms (n = 250)

	Mean (SD)	Min.	Max.
CRI, cognitive	27.2 (5.0)	11	36
CRI, social	40.4 (5.7)	23	52
CRI, emotional	45.3 (8.0)	24	63
CRI, spiritual	27.5 (5.2)	13	43
CRI, physical	27.6 (4.8)	13	38
HADS, anxiety ^a	7.1 (4.3)	0	20
HADS, depression ^b	4.8 (3.5)	0	16
VSI	34.6 (16.6)	4	72
SCL90-R, somatization	11.2 (7.6)	0	36
GSRS, total	3.2 (0.84)	1.2	5.4

GSRS, Gastrointestinal Symptom Rating Scale; HADS, Hospital Anxiety and Depression Scale; SCL-90R, Symptom Check List-90 Revised; SD, standard deviation; VSI, Visceral Sensitivity Index.

^a43 of 250 (17.2%) patients had HAD anxiety score >10, hence clinically significant anxiety.

^b17 of 250 (6.8%) patients had HAD depression score >10, hence clinically significant depression.