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SCIENTIFIC INVESTIGATIONS

Indirect effect of sleep on abdominal pain through daytime dysfunction in adults with irritable bowel syndrome

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Study Objectives: Sleep deficiency, psychological distress, daytime dysfunction, and abdominal pain are common in adults with irritable bowel syndrome. Prior research on individuals with chronic pain has identified the indirect effect of sleep on pain through psychological distress or daytime dysfunction; however, this effect is less clear in irritable bowel syndrome. The purpose of this study was to examine potential indirect effects of sleep on abdominal pain symptoms simultaneously through psychological distress and daytime dysfunction in adults with irritable bowel syndrome.

Methods: Daily symptoms of nighttime sleep complaints (sleep quality and refreshment), psychological distress, daytime dysfunction (fatigue, sleepiness, and difficulty concentrating), and abdominal pain were collected in baseline assessments from 2 randomized controlled trials of 332 adults (mean age 42 years and 85% female) with irritable bowel syndrome. Structural equation modeling was used to examine the global relationships among nighttime sleep complaints, psychological distress, daytime dysfunction, and abdominal pain.

Results: The structural equation modeling analyses found a strong indirect effect of poor sleep on abdominal pain via daytime dysfunction but not psychological distress. More than 95% of the total effect of nighttime sleep complaints on abdominal pain was indirect.

Conclusions: These findings suggest that the primary impact of nighttime sleep complaints on abdominal pain is indirect. The indirect effect appears primarily through daytime dysfunction. Such understanding provides a potential avenue to optimize personalized and hybrid behavioral interventions for adults with irritable bowel syndrome through addressing daytime dysfunction and sleep behaviors. Additional study integrating symptoms with biological markers is warranted to explore the underlying mechanisms accounting for these symptoms.

Clinical Trial Registration: Registry: ClinicalTrials.gov. Name: Nursing Management of Irritable Bowel Syndrome: Improving Outcomes, Nursing Management of IBS: Improving Outcomes. URLs: https://clinicaltrials.gov/ct2/show/NCT00167635, https://clinicaltrials.gov/ct2/show/NCT00907790. Identifiers: NCT00167635, NCT00907790.

Keywords: irritable bowel syndrome, sleep, pain, daytime dysfunction, psychological distress

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Prior research on multiple populations with chronic pain has identified an indirect effect of sleep on pain through psychological distress or daytime dysfunction (ie, fatigue, sleepiness). However, these indirect effects on the sleep-pain relationship in adults with irritable bowel syndrome are less clear.

Study Impact: This study supports a strong indirect effect of poor sleep on abdominal pain via daytime dysfunction, but not psychological distress, in adults with irritable bowel syndrome. Such an understanding provides a new window to develop effective and hybrid interventions for adults with irritable bowel syndrome through addressing sleep behaviors and daytime functioning.

INTRODUCTION

Irritable bowel syndrome (IBS) is a prevalent chronic functional bowel disorder worldwide, characterized by chronic, recurrent abdominal pain/discomfort related to defecation or a change in bowel habits (constipation and/or diarrhea).[1,2] Adults with IBS often experience gastrointestinal symptoms (ie, abdominal pain, constipation and/or diarrhea, abdominal bloating and distension), and nongastrointestinal symptoms (eg, sleep deficiency, psychological distress, daytime dysfunction).[1,3] IBS adversely impacts health-related quality of life and work productivity.[4–8] In the United States, the estimated direct medical costs of IBS (ie, outpatient care, primary and specialist physician visits) are between $1.7 and $10 billion/year, and the estimated indirect costs (ie, productivity loss, work productivity, quality of life) are $20 billion. There is an urgent need to identify modifiable risk factors to design effective treatments for adults with IBS.[8]

Sleep deficiency is a well-documented health concern in adults living with IBS, affecting an estimated 37.6% of this population.[9,10] Sleep deficiency is a broad concept, encompassing both sleep deprivation and poor sleep quality.[11] Researchers using both self-reported and objective measures have shown that poor sleep quality is a significant predictor of next-day IBS symptoms (ie, abdominal pain/discomfort), psychological distress

(ie, depression, anxiety), and daytime dysfunction (ie, fatigue and sleepiness).[12–16] Poor sleep quality is a modifiable risk factor for IBS symptom flare-ups, particularly for abdominal pain, which is the most bothersome of IBS symptoms.[17–19]

Systematic reviews of the sleep-pain relationship have revealed an indirect effect of sleep on pain through psychological distress or daytime dysfunction in individuals with chronic pain-related conditions such as fibromyalgia, rheumatoid arthritis, abdominal pain, or headache.[20,21] However, less is known about the roles of psychological distress and daytime dysfunction in the sleep-pain relationship in adults with IBS. Limited evidence in IBS has suggested an indirect effect of sleep on pain through psychological distress. One study in 24 adults with IBS found that the effect of poor sleep quality (indicated by waking episodes measured by a wrist-worn actigraph) on self-reported abdominal pain symptoms was partially mediated by psychological distress.[13]

Even less is known about the indirect effect of sleep on pain through daytime dysfunction in persons with IBS. In a study of 918 female adolescents, Bonvanie and colleagues[22] found that self-reported poor sleep quality indirectly affected abdominal pain through fatigue (1 component of daytime dysfunction); however, the investigators did not adjust for the potential confounding effect of psychological distress. Taken together, prior studies have not simultaneously evaluated the potential indirect effects of sleep on pain through both psychological distress and daytime dysfunction.

Sleep deficiency, abdominal pain, daytime dysfunction, and psychological distress are common in individuals with IBS,[3,12,23] so clarifying the roles of varied factors in the sleep-pain pathway in persons with IBS could have significant clinical implications for the management of symptom clusters. The purpose of this study was to examine the potential indirect effects of sleep on pain through psychological distress and/or daytime dysfunction among adults with IBS by using a structural equation modeling (SEM) approach. SEM allows for the inclusion of multiple indicators to measure the multifaceted symptom constructs of sleep deficiency, psychological distress, daytime dysfunction, and abdominal discomfort/pain,[3,20,21] and further to reduce measurement error of these 4 multifaceted symptoms of interest.[24] In addition, SEM can include analyses of multiple relationships simultaneously (ie, direct and indirect effects) to build a more sophisticated statistical model rather than doing several individual regressions.[24,25] Utilizing SEM may provide a unique window into the understanding of how sleep deficiency, abdominal discomfort/pain, daytime dysfunction, and psychological distress interact to optimize symptom management in IBS populations.

METHODS

Participants

This study is a secondary data analysis using baseline symptom diary data recorded over 28 consecutive days from 2 randomized controlled trials (RCTs) among adults with IBS. This study includes a total sample of 332 adults with IBS (RCT-1 = 224; RCT-2 = 108), both previously described in detail elsewhere and registered on ClinicalTrials.gov of the National Institutes of Health (Clinicaltrials.gov identifiers: NCT00167635 for RCT 1; NCT00907790 for RCT 2).[26,27] Participants were recruited through community advertisements. Both RCTs applied similar eligibility criteria: (1) a medical diagnosis of IBS and symptoms compatible with Rome II[28] (for RCT-1) or III[29] (for RCT-2) criteria for IBS; (2) ages 18–70 years; (3) no significant comorbidity based on the guiding principle of whether the morbidity could affect symptom measures or compromise a participant's ability to complete the study (ie, symptoms of cognitive impairments, untreated sleep disorder, severe depression, and a moderate to severe pain disorder); and (4) not taking medications that could affect outcome measures (ie, antidepressants, calcium-channel blockers, anticholinergics, cholestyramine, narcotics, colchicine, iron supplements, or laxatives).

Measures

Daily symptom measures of abdominal discomfort/pain, psychological distress, and daytime function

All participants completed a daily 26-item symptom diary every evening over 28 consecutive days (over 1 menstrual cycle).[26,27] The severity of each daily IBS symptom over the past 24 hours was rated on a scale of 0 (not present), 1 (mild), 2 (moderate), 3 (severe), or 4 (very severe). Items included in the analyses were ratings of abdominal discomfort/pain (abdominal pain, abdominal pain after eating, abdominal distention, intestinal gas), psychological distress (depressive mood, anxiety, stress), and daytime dysfunction (fatigue, sleepiness during the day, difficulty concentrating). Acceptable construct validity of the 26-item symptom diary has been confirmed by previous IBS studies.[3,30,31]

Daily sleep measures

Participants also daily assessed overall sleep quality and feelings of "refreshed sleep" at the same time as the daily symptom diary was completed. Participants evaluated overall sleep quality as poor, fair, good, very good, or excellent and rated the item "I felt refreshed by last night's sleep" as "not at all refreshed," "somewhat refreshed," "moderately refreshed," or "very refreshed." The responses showed appropriate validity when correlated with validated sleep measures.[32–34]

Statistical analyses

All symptom measures were represented by the percentage of symptomatic days in the 28-day diary. For indicators of abdominal discomfort/pain, psychological distress, and daytime dysfunction, symptomatic days were indicated by ratings of 2 (moderate) to 4 (very severe) (100% × number of days with a rating of ≥ 2/28 symptomatic days).[3] For sleep quality, a rating of poor or fair indicated nights with poor sleep, and for refreshing sleep, "not at all refreshing" or "somewhat refreshing" indicated nights with unrefreshing sleep.[35] Using the percentage of symptomatic days over 28-day diary data for each indicator allowed us not only to capture both the symptom severity and frequency but also to minimize recall bias from self-report measures. All measures were collected at baseline and before any intervention.

Table 1—Descriptive statistics and zero-order correlations.

Measure	Mean	(SD)	1	2	3	4	5	6	7	8	9	10	11	12
Age, y	42.18	(14.61)	–	–	–	–	–	–	–	–	–	–	–	–
Female (1 = yes)	0.85	(0.36)	–	–	–	–	–	–	–	–	–	–	–	–
Outcomes														
Abdominal discomfort/pain														
1. Abdominal pain	37.08	(26.05)	–											
2. Abdominal pain after eating	29.64	(26.01)	.80	–										
3. Abdominal distention	31.01	(31.82)	.66	.68	–									
4. Intestinal gas	38.67	(30.05)	.57	.55	.62	–								
Predictors														
Nighttime sleep complaints														
5. Diminished sleep quality	40.65	(27.18)	.25	.25	.20	.22	–							
6. Unrefreshed sleep	48.61	(27.15)	.20	.22	.18	.21	.81	–						
Daytime dysfunction														
7. Fatigue	33.98	(27.25)	.45	.42	.40	.38	.39	.42	–					
8. Sleepiness during the day	26.43	(25.79)	.44	.43	.39	.35	.35	.36	.83	–				
9. Hard to concentrate	13.93	(20.77)	.35	.33	.32	.30	.27	.30	.62	.60	–			
Psychological distress														
10. Anxiety	18.76	(22.41)	.31	.25	.19	.30	.18	.18	.44	.43	.51	–		
11. Stress	25.64	(25.44)	.39	.35	.29	.28	.24	.25	.58	.58	.55	.75	–	
12. Depressive mood	9.64	(16.51)	.26	.25	.13	.20	.15	.17	.43	.43	.60	.70	.62	–

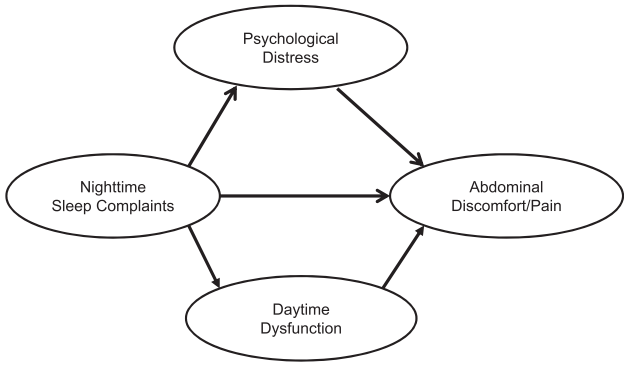
N = 332 adults with irritable bowel syndrome. Pearson's *r* reported. Means (SDs) for abdominal discomfort/pain, daytime dysfunction, and psychological distress indicators are the symptom severity for each indicator, defined as the percentage of days rated as "moderate" to "very severe" of each symptom severity over 28 days. Mean (SD) for diminished sleep quality indicator is defined as the percentage of days rated as having poor to fair sleep quality over 28 days. Mean (SD) for unrefreshed sleep indicator is defined as the percentage of days rated as having "not at all refreshed" or "somewhat refreshed" sleep over 28 days. All correlation coefficients are significant at $P < .01$. SD = standard deviation.

Descriptive statistics were used to describe the demographic and clinical characteristics of the participants and all indicators of the latent variables of nighttime sleep complaints, abdominal discomfort/pain, daytime dysfunction, and psychological distress (see **Table 1**).

The statistical analyses were performed in 2 phases.[24] In the first phase, confirmatory factor analysis was used to evaluate the validity of the hypothesized measurement model. Latent variables were free to covary without specifying structural relationships. Sequentially, the measurement invariance of the established measurement model was evaluated to examine moderating effects of the 2 parent studies (RCT-1 and RCT-2) and sex. Such tests of measurement invariance aimed to determine if combining the samples of the 2 parent studies in the analyses was appropriate and to determine the need for doing separate analyses based on sex. Therefore, we examined the measurement invariance of the final model across groups including the 2 parent studies and sex by comparing the model of configural invariance with the model of metric invariance.[36] Next, chi-square difference tests were used to determine whether the model of metric invariance would improve the goodness-of-fit index (GFI) of the measurement model.

In the second phase, SEM was used to examine the relationships among the 4 latent variables and to test hypotheses about the direct and indirect effects of sleep on pain through psychological distress and/or daytime dysfunction (**Figure 1**). In both phases, the GFI including the chi-square, the comparative fit index (CFI), the standardized root mean-square residual (SRMR), and the root mean-square error of approximation (RMSEA) with 90% confidence interval were used to assess how well the models fit the dataset. The recommended cutoff of CFI is ≥ 0.90. A SRMR > 0.10 indicates a poor fit, and an

Figure 1—Initial hypothesized structural model of direct and indirect effects of sleep on pain through psychological distress and daytime dysfunction.



Latent variables are represented in ovals.

RMSEA < 0.08 indicates an acceptable fit.[37] The statistical software package RStudio version 3.6.1 under the lavaan statistical package was used for CFA and SEM with maximum likelihood estimation.

RESULTS

Descriptive statistics and correlations between symptom indicators

Of the 1,498 potential participants screened for the 2 parent studies (RCT-1 = 771; RCT-2 = 727),[26,27] 1,166 persons (RCT-1 = 547; RCT-2 = 619) were excluded in this data analysis for various reasons (ie, did not meet inclusion criteria, declined to participate, did not respond to call). A total sample of 332 adults with IBS were included in this study. Demographic and clinical characteristics of the sample were previously described in detail elsewhere.[3] The mean age of the participants was 42.18 ± 14.61 years, and 85% were women. Most participants were racially self-identified as White (80.4%) and college-educated (84.3%) (data not shown). **Table 1** summarizes the descriptive statistics and correlations of the measures.

Measurement model

Table 2 presents the unstandardized and standardized factor loadings of the symptom indicators for the latent variables and GFI in our measurement model. Our measurement model yielded an acceptable fit to the dataset (CFI = 0.95; RMSEA = 0.09 [90% CI, 0.08–0.10]; $P < .001$; SRMR = 0.05). Standardized factor loadings of symptom indicators within their latent variables (ie, nighttime sleep complaints, daytime dysfunction, psychological distress, and abdominal discomfort/pain) were all statistically significant and > 0.6, suggesting that the latent variables were measured adequately by their respective symptom indicators.

Measurement invariance

Table 3 presents the GFI of tests of measurement invariance by group. The measurement model was invariant across the 2 parent studies (RCT-1 and RCT-2) and sex, indicating that the measurement model was valid for participants in both the RCT-1 and RCT-2 studies and regardless of sex.

SEM model

Figure 2 illustrates the standardized estimates for structural relationships and factor loadings for each indicator of the initial SEM model. The GFI of the initial SEM model (CFI = 0.91; RMSEA = 0.12 [90% CI, 0.11–1.14]; $P < .001$; SRMR = 0.16) suggested an inadequate model fit. Based on modification index values, a direct path between psychological distress and daytime dysfunction was added and was also supported by empirical evidence.[23]

Table 2—Summary of the measurement model from confirmatory factor analysis.

Latent Variable	Indicator	Unstandardized Factor Loading	Standardized Factor Loading	Standard Error	GFI Indexes	P^a
Abdominal discomfort/pain	Abdominal pain	22.97	.88	1.16		
	Abdominal pain after eating	22.93	.88	1.16		
	Abdominal distention	24.73	.78	1.52		
	Intestinal gas	20.17	.67	1.52		
Nighttime sleep complaints	Diminished sleep quality	23.94	.88	1.49		
	Unrefreshed sleep	25.02	.92	1.48		
Daytime dysfunction	Fatigue	25.04	.92	1.18		
	Sleepiness during the day	23.09	.90	1.13		
	Hard to concentrate	14.37	.69	1.03		
Psychological distress	Anxiety	19.03	.86	1.04		
	Stress	22.13	.87	1.18		
	Depressive mood	12.47	.76	0.81		
Measurement model fit indexes						
Chi-square (df)					174.09 (48)	< .001
CFI					0.95	
SRMR					0.05	
RMSEA					0.09	< .001
RMSEA 90% CI—lower					0.08	
RMSEA 90% CI—upper					0.10	

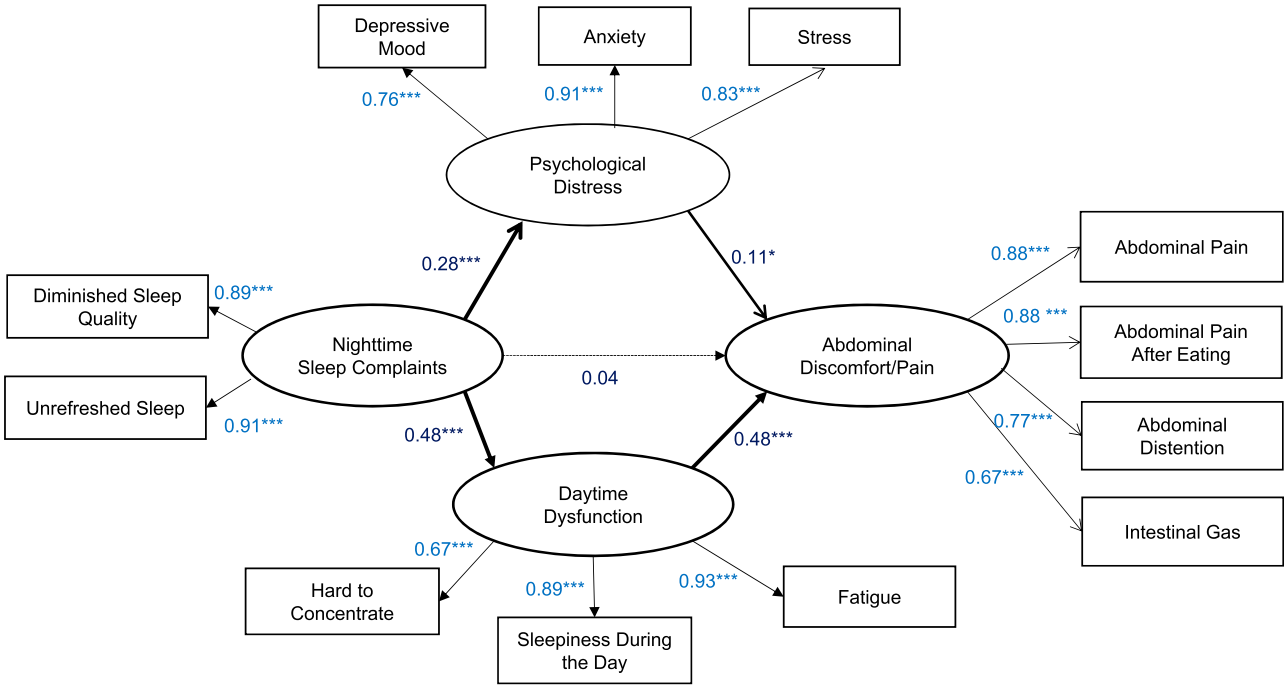
N = 332 adults with irritable bowel syndrome. All loadings based on maximum likelihood estimates. All loadings are significant at $P < .001$; P^a is for measurement model fit indexes of $\chi 2$ and RMSEA. CFI = comparative fit index, CI = confidence interval, df = degree of freedom, GFI, goodness-of-fit, RMSEA = root mean-square error of approximation, SRMR = standardized root mean-square Residual.

Table 3—Fit statistics for tests of group invariance.

Model	Chi-Square	df	CFI	RMSEA	SRMR	BIC	Change in Chi-Square	Change in df	P^a
RCT-1 (n = 224) vs. RCT-2 (n = 108)									
Configural invariance	248.64	96	0.942	0.098	0.055	34976			
Metric invariance with all loadings constrained equal	253.42	104	0.943	0.093	0.055	34934	4.778	8	.781
Women (n = 283) vs men (n = 49)									
Configural invariance	233.57	96	0.947	0.093	0.052	34903			
Metric invariance with all loadings constrained equal	240.61	104	0.947	0.089	0.053	34864	7.039	8	.53

P^a is for chi-square difference tests. BIC = Bayesian information criterion, CFI = comparative fit index, df = degree of freedom, RCT = randomized controlled trials, RMSEA = root mean-square error of approximation, SRMR = standardized root mean-square residual.

Figure 2—Initial structural model of nighttime sleep complaints, psychological distress, daytime dysfunction, and abdominal discomfort/pain symptoms in adults with irritable bowel syndrome.

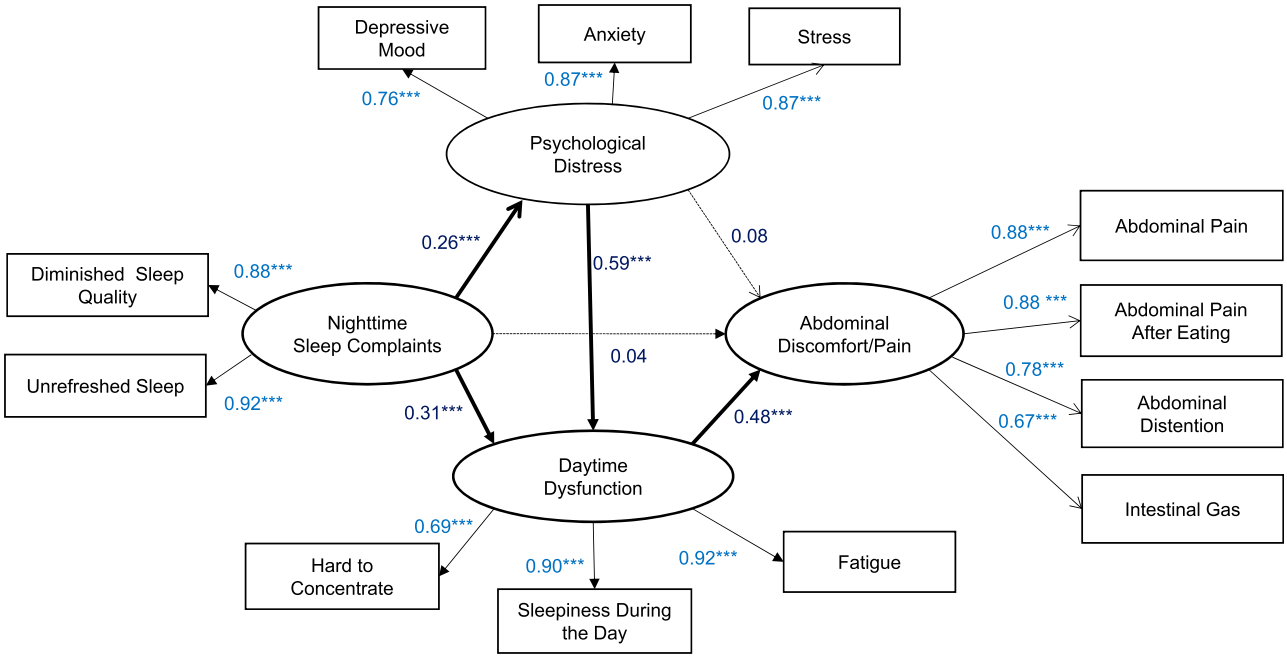


Latent variables are represented in ovals, and indicators of latent variables are represented in rectangles. Standardized factor loadings (in light blue) of symptom indicators within their latent variables from confirmatory factor analyses were all statistically significant and > 0.6, suggesting that the latent variables were measured adequately by their respective symptom indicators. The standardized estimates (in dark blue) represent structural pathway relationships between the latent variables from SEM analyses. However, this initial SEM model yielded inadequate model fit. Solid lines indicate significant paths; dashed lines indicate nonsignificant paths. SEM = structural equation modeling. *P < .05, ***P < .001.

The final SEM model (**Figure 3**) yielded a relatively good model fit to the data (CFI = 0.95; RMSEA = 0.09 [90% CI, 0.08–0.10]; P < .001; SRMR = 0.05). Nighttime sleep complaints were a significant predictor for psychological distress (β = 0.26; P < .001) and daytime dysfunction (β = 0.31; P < 0.001) but not for abdominal discomfort/pain (β = 0.04; P = .621). Similarly, psychological distress was a significant predictor for daytime dysfunction (β = 0.59; P < .001) but not for abdominal discomfort/pain (β = 0.08; P < .301). Daytime dysfunction was significantly predictive for abdominal discomfort/pain (β = 0.48; P < .001).

Table 4 summarizes the indirect and direct effects on the relationship of nighttime sleep complaints to abdominal discomfort/pain through psychological distress and daytime dysfunction in the initial and final SEM models. In both models, there was a specific positive indirect relationship of nighttime sleep complaints with abdominal discomfort/pain significantly linked to daytime dysfunction (initial SEM model: β = 0.23; P < .001; final model: β = 0.74; P < .001) but not significantly linked to psychological distress (initial SEM model: β = 0.03; P = .068; final model: β = 0.02; P = .315). The total effect of nighttime sleep complaints on abdominal discomfort/pain was significantly positive in both models (initial SEM model: β = 0.30; P < .001; final model: β = 0.80; P < .001). In addition, the direct effect of

Figure 3—Final structural model of nighttime sleep complaints, psychological distress, daytime dysfunction, and abdominal discomfort/pain symptoms in adults with irritable bowel syndrome.



Given inadequate model fit of the initial SEM model, a direct path between psychological distress and daytime dysfunction was added to create this SEM model, which then yielded relatively good model fit. Nighttime sleep complaint was a significant predictor for psychological distress (β = 0.26) and daytime dysfunction (β = 0.31) but not for abdominal discomfort/pain (β = 0.04). Psychological distress was a significant predictor for daytime dysfunction (β = 0.59) but not for abdominal discomfort/pain (β = 0.08). Daytime dysfunction was significantly predictive for abdominal discomfort/pain (β = 0.48). Latent variables are represented in ovals, and indicators of latent variables are represented in rectangles. The standardized estimates (in dark blue) represent structural pathway relationships between the latent variables from SEM analyses. Solid lines indicate significant paths; dashed lines indicate nonsignificant paths. SEM = structural equation modeling. *P < .05, ***P < .001.

Table 4—Analysis of direct and indirect effects of sleep on pain.

		Outcome Variable			
		Abdominal Discomfort/Pain			
Predictor Variable	**Mediator**	**Indirect Effect**	**Total Indirect Effect**	**Direct Effect**	**Total Effect**
Initial SEM model					
Nighttime sleep complaints	Psychological distress	0.03	0.26***	0.04	0.30***
	Daytime dysfunction	0.23***			
Final SEM model					
Nighttime sleep complaints	Psychological distress	0.02	0.76***	0.04	0.80***
	Daytime dysfunction	0.74***			

***P < .001. SEM = structural equation modeling.

nighttime sleep complaints on abdominal discomfort/pain was not statistically significant (initial SEM model: β = 0.04; P = .531; final model: β = 0.04; P = .621). Taken together, the path of nighttime sleep complaints to abdominal discomfort/pain was through daytime dysfunction but not through psychological distress.

DISCUSSION

This study is the first to examine the potential indirect effects of sleep on pain through psychological distress and daytime dysfunction symptoms simultaneously in community-dwelling adults with IBS. The results of this study suggest that the primary impact of nighttime sleep complaints on abdominal discomfort/pain symptoms is indirect through daytime dysfunction. That is, a higher severity of nighttime sleep complaints seems to increase the severity of psychological distress and daytime dysfunction. Sequentially, a higher severity of daytime dysfunction seems to perpetuate the impact of nighttime sleep complaints on abdominal discomfort/pain symptoms in adults with IBS. As such, the sleep-pain relationship in adults with IBS is significantly attenuated by an individual's perception of better daytime functioning.

The current evidence regarding the nonsignificant direct effect of poor sleep quality on abdominal discomfort/pain coincides with our previous findings in which actigraphic sleep efficiency was not predictive for next-day abdominal discomfort/pain across and within adult patients.[12] In addition, the indirect effect of sleep through daytime dysfunction may explain previous findings in which effects of self-reported poor sleep quality on abdominal discomfort/pain symptoms only existed "within" patients but not "across" patients.[12] The indirect effect of sleep through daytime dysfunction could reflect inadequate coping strategies for daytime dysfunction symptoms[38] or an individual trait (ie, catastrophizing)[39] toward globally reporting multiple symptoms with consistent severity ratings.[40] This effect may explain why comprehensive self-management including cognitive-behavioral therapy is effective for alleviating abdominal discomfort/pain for adults with IBS.[26,27] However, there may also be a physiological pathway by which sleep dysfunction concurrently disrupts daytime function and also sensitizes the central nervous system to abdominal pain sensations.[41–43]

Daytime dysfunction symptoms are well-known consequences of sleep deficiency[44] and have also been previously linked with abdominal discomfort/pain symptoms. Two prospective population-based studies found that fatigue[45] or daytime tiredness[46] were significant predictors of the onset of abdominal pain. A population-based study in China found that persons with excessive daytime sleepiness were more likely to experience functional gastrointestinal disorders on the basis of Rome II criteria.[47] Similarly, "hard to concentrate" as a proxy for daytime dysfunction was also found to be associated with IBS-related discomfort and pain symptoms while initiating and/or maintaining sleep.[48] Our current findings about the indirect effect of sleep on pain through daytime dysfunction reveal that the presence of daytime dysfunction symptoms provides a significant variance in the sleep-pain relationship in persons with IBS.

In contrast to the present findings, a prior study by Patel and colleagues[13] identified the indirect effect of sleep on pain through psychological distress in 24 adults with IBS. Such a discrepancy might be attributed to methodological differences and/or patient characteristics between their study and this one. For example, Patel et al[13] used multiple retrospective measures of psychological distress, which may have been influenced by recall bias, and a prospective objective measure of sleep (actigraphy). The current study used prospective daily symptom diaries to assess both psychological distress and sleep.[40] It may be that the self-reported sleep measures in our study compared to the actigraphic sleep measures in Patel et al[13] may capture different aspects of the sleep-pain relationship. The potential indirect effect of sleep on pain through psychological distress should be confirmed by a larger study that concurrently applies self-reported and physiological sleep measures in IBS.

The findings of this study have important implications for understanding and managing IBS symptoms. Because nighttime sleep complaints directly predicted both daytime dysfunction and psychological distress, treating nighttime sleep complaints may alleviate both of these symptom clusters. However, an intervention only targeting sleep without taking account of daytime function (fatigue, tiredness, cognitive dysfunction) may be less effective for treating abdominal discomfort/pain. Addressing daytime dysfunction seems to be an even more critical target of IBS symptom management among adults with IBS who experience both nighttime sleep complaints and abdominal discomfort/pain (with and without psychological distress). Based on existing evidence in other populations with chronic conditions such as cancer[49–51] and rheumatic diseases,[52] the underlying mechanisms of the sleep-pain relationship through daytime dysfunction remain unclear in IBS. Inflammation (ie, high levels of interleukin-6 or tumor necrosis factor-α), the hormones of the hypothalamic-pituitary-adrenal axis system, and neurotransmitter dysregulation may be involved. For example, sleep dysfunction has been found to activate the immune system and significantly increase proinflammatory cytokine (interleukin-6, tumor necrosis factor-α) levels,[53] which could signal the central nervous system and lead to daytime dysfunction symptoms (ie, fatigue) or other behavioral changes.[51] There is also evidence indicating that inflammation has adverse effects on pain experience (ie, visceral hyperalgesia) through the dysregulation of the hypothalamic-pituitary-adrenal axis system and/or the autonomic nervous system, which may result from the indirect effect of sleep dysfunction through fatigue.[52] Such proposed mechanisms have been supported by a meta-analysis in which interleukin-6 levels were higher in individuals with IBS than in healthy control patients.[54] Whether there is a shared mechanism linking sleep with abdominal discomfort/pain through daytime dysfunction in adults with IBS is still a question that bears further research to integrate symptoms with biological markers.

LIMITATIONS

Despite our findings that add to current knowledge regarding the relationship of nighttime sleep complaints and abdominal pain in adults with IBS, there are limitations in the current study. The study used a community sample of adults with IBS, and the majority were women. The relationships in the current SEM model may vary when different patient characteristics are analyzed. For example, a study in 871 adults with IBS found that the correlations between daytime dysfunction (indicated by driving lapses) and IBS-like pain symptoms only existed in women but not in men.[48] Therefore, replication in more diverse IBS patients including more men with IBS or those with additional comorbidities is warranted. In addition, although the directional relationships among the latent variables of nighttime sleep complaints, psychological distress, daytime dysfunction, and abdominal discomfort/pain in the hypothesized SEM model were supported by our prior sleep studies of women only with IBS,[12,15] this study utilized a cross-sectional SEM approach and thus temporal sequences among these latent variables in IBS could not be established because of the current sample size limitations. There may be alternative models fitting the data equally well. For example, another alternative SEM model of the direct and indirect effect of sleep on daytime dysfunction through psychological distress and abdominal discomfort/pain symptoms could be considered as well. The directionality of

these causal relationships in IBS needs confirmation by experimental research or a cross-lagged panel analysis in a prospective study design with a large sample size. This study aimed to examine a hypothesized model that was supported by the data to test the global relationships among sleep, pain, psychological distress, and daytime dysfunction among adults with IBS.Despite this limitation of temporal sequencing, this study has made a significant contribution by simultaneously testing multiple direct and indirect effects of sleep on pain through psychological distress and daytime dysfunction, and it found a strong indirect effect only through daytime dysfunction but not through psychological distress. This study also differs from previous studies in the utilization of multiple indicators and its account for measurement errors. Because of the lack of the information about the quantity of sleep obtained from the parent studies, our results may only support the direct and indirect effects of poor sleep quality on abdominal pain. We suggest that future studies add an indicator related to inadequate amount of sleep to capture a comprehensive picture of sleep deficiency among these symptom relationships of interest. Given the nature of this secondary analysis, symptom data were obtained from daily diary responses. Future researchers may consider adding other validated parallel indicators (eg, the patient-reported outcomes information system gastrointestinal symptom scales, the Pittsburgh Sleep Quality Index)[55] to verify our SEM models. Symptom data in the current study relied on self-report measures rather than objective measures (ie, actigraphy for sleep, provocation tests for abdominal pain). Even though these elements are considered limitations, symptoms are self-reported individual experiences; therefore, self-report may be an appropriate measurement for symptoms. Our results are limited to understanding the relationships among self-perceived symptoms (ie, sleep, pain, psychological and daytime functioning) in IBS.

CONCLUSIONS

Findings from our SEM analyses show a strong indirect effect of nighttime sleep complaints on abdominal pain through daytime dysfunction in adults with IBS, suggesting that daytime dysfunction is a critical target for IBS symptom management. Among adults with IBS, adequate daytime functioning could essentially reduce or remove poor sleep during the night as a risk factor for abdominal discomfort/pain symptoms even after adjusting for psychological distress. If adults with IBS experience poor sleep quality and/or psychological distress but they can maintain appropriate daytime functioning, then the impact of poor sleep on abdominal discomfort/pain can be minimized. Our findings add to current knowledge about patients with IBS by linking nighttime sleep complaints to abdominal discomfort/pain through daytime dysfunction, and they provide a potential avenue to optimize personalized and hybrid intervention through addressing daytime functioning and sleep behaviors for IBS populations. Additional work is warranted to address the issue of causality and directionality and to understand a shared mechanism among these symptom constructs.

ABBREVIATIONS

CFA, confirmatory factor analysis
CFI, comparative fit index
GFI, goodness of fit index
IBS, irritable bowel syndrome
RCT, randomized controlled trials
RMSEA, root mean-square error of approximation
SEM, structural equation modeling
SRMR, tandardized root mean-square residual

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