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An Initial Report of Sleep Disturbance in Inactive Inflammatory Bowel Disease

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Background: There is an increased prevalence of gastrointestinal symptoms, peptic ulcer disease, and colon cancer in night-shiftworkers, whose sleep is commonly disrupted. Sleep complaints are an extrapyramidal symptom of irritable bowel syndrome (IBS). Sleep disruption may contribute to increased medical morbidity by weakening the ability of the immune system to protect against endotoxins—this pathway could be of potential importance to the pathogenesis and/or clinical course of inflammatory bowel disease (IBD), a chronic immunoinflammatory gastrointestinal disorder associated with marked reductions in quality of life. This is the first study to comprehensively examine sleep concerns in patients with IBD.

Methods: Sixteen patients with biopsy-proven inactive IBD (8 with Crohn disease and 8 with ulcerative colitis), 9 patients with IBS, and 7 healthy controls completed the Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, Inflammatory Bowel Disease Questionnaire, SF-12, and a single overnight polysomnogram. Polysomnography and arousals were scored according to standard criteria. Multivariate analyses were used to compare subjective and objective sleep parameters between groups and to identify associations between sleep complaints and quality of life.

Results: Patients with IBD did not seem to significantly differ from patients with IBS, who have established sleep complaints. On polysomnography, total sleep time differentiated the 3 groups well, with the IBS and IBD groups appearing numerically similar. Whereas IBS and IBD groups were similar with respect to observed sleep parameters, IBS patients did report the most concerns, consistent with earlier research suggesting that hyperarousal and perceptual differences may contribute to symptom reporting.

Conclusion: Sleep parameters greatly influenced quality of life in both groups and highlight the need to address sleep concerns as part of IBD management.

Keywords: Inflammatory bowel disease, irritable bowel syndrome, sleep disturbances, quality of life

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Chronic sleep disruption has been identified as a risk factor for heart attack,[1] cardiovascular disease,[2] and metabolic and endocrine disorders.[3] Less is known about the effects of sleep disruption on gastrointestinal function. This is of interest given the increased prevalence of gastrointestinal symptoms,[4] peptic ulcer disease,[5] and colon cancer[6] in night-shift workers, whose sleep is commonly disrupted. One way in which sleep disruption may contribute to increased medical morbidity is by weakening the ability of the immune system to protect against endotoxins.[7]

There are several studies to support associations between sleep, immune function, and inflammation.[8] First, activation of the host immune system will lead to alterations in the sleep-wake cycle.[9,10] Specifically, inflammatory cytokines interleukin (IL)-1 and tumor necrosis factor (TNF) have been shown to promote slow-wave sleep (SWS) in animal studies,[11-14] and the proinflammatory cytokine IL-6 has been important in promoting periods of wakefulness.[11] Bacterial endotoxins have been shown to disturb sleep in high doses[8] and promote non-rapid eye movement (REM) sleep in low doses.[8] Finally, patients with immunoinflammatory diseases, including lupus erythematosus,[15] multiple sclerosis,[16] rheumatoid arthritis[17] and HIV,[18] often exhibit sleep abnormalities, including increased sleepiness, fatigue, and impaired daytime function.

Conversely, sleep restriction has been associated with secretion of proinflammatory cytokines IL-6 and TNF-α and increases in the inflammatory marker C-reactive protein.[19,20] In animal models, it has also been associated with unexplained hypercatabolic states, malnutrition symptoms, and mortality.[10] After sleep loss, there are elevations in granulocytes and monocytes,[7,9] and, with sustained sleep deprivation, there are increases in natural killer cells and monocytes, which form the basis for the secretion of inflammatory cytokines.[9] Finally, sleep significantly affects the propagating and nonpropagating activity in the colon—during SWS, propagating contractions are eliminated and the colon remains inactive. However, during arousals and upon waking, there are immediate stimulatory effects on colonic motility.[21-23] The implications of this in inflammatory bowel disease (IBD) are important—if patients are not obtaining SWS due to frequent arousals, their intestinal tract has limited time to recover. Further, frequent arousals could lead to symptom exacerbation through increased colonic motility.[21-23]

Thus, it is reasonable to hypothesize that sleep disturbance

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could negatively influence the clinical course of disorders that exhibit gut inflammation. Some of the most common and clinically important inflammatory disorders of the gut are IBDs, the clinical course of which are marked by symptomatic periods (flare-up) interspersed with asymptomatic periods (remission).[24] The 2 most common IBDs are Crohn's disease and ulcerative colitis. These disorders typically present in young adults and have a considerable impact on quality of life (QOL) and work productivity.[24] During flare-up (active disease), patients suffer from embarrassing and disabling symptoms such as bloody diarrhea, abdominal pain, fecal incontinence, fatigue, fever, arthritis, or arthralgia, or a combination of these symptoms.[24]

Although the etiology of IBD is unknown, it has been fairly well established that leakiness of the epithelial mucosal barrier may contribute to continued stimulation of the immune system by luminal factors and bacteria,[25] creating a vicious cycle of perpetually recurring inflammation. Increased exposure of bacterial antigens to the immune system results in a sustained inflammatory cascade through continuous production of proinflammatory cytokines, namely IL-1, IL-6, and TNF-α. During a disease flare-up, the intestinal mucosa is abnormal, with evidence of active inflammation and tissue injury manifested by mucosal ulcerations that can be readily observed on endoscopy.[26] Histologically, the inflamed colonic mucosa contains large numbers of lymphocytes and neutrophils (polymorphonuclear leukocytes), and there is evidence of tissue destruction.[26]

Sleep disturbances, if present in patients with IBD, could have significant deleterious effects on disease course and important practical implications for disease management. First, immunologic and inflammatory responses to sleep disruption may potentate the inflammatory cascade and initiate or exacerbate flare-up in IBD. Second, disruptions in sleep and wakefulness during a flare-up may impact response to treatment, influence QOL and affect productivity. The potential deleterious effects of disrupted sleep on gut function could worsen symptoms such as diarrhea and abdominal pain independent of the effects of disrupted sleep on inflammation.

The aim of this study was to precisely characterize the nature of sleep disturbances in patients with IBD and the association of these disturbances with disease outcomes, including QOL. We recruited 16 patients with inactive IBD and compared data obtained from these participants with data from 2 control groups—patients with irritable bowel syndrome (IBS) and healthy individuals. We chose patients with IBS as a "positive symptom control" group to enhance internal validity in this study. IBS serves as a useful comparison group for a few reasons: (1) IBS is a prevalent[27] intestinal disorder characterized by altered bowel habits and recurrent abdominal pain in the absence of any recognized organic gastrointestinal pathology; (2) as in IBD, the course of IBS is recurring and chronic with considerable variability in symptom presentation, with symptoms that wax and wane with stress[28]; and (3) disrupted sleep has been well documented in IBS populations.[29-32] Although the etiology of IBS is unknown, it is widely believed that IBS is a 3-component disorder that includes central nervous system hyperarousal, abnormalities in visceral motor activity, and altered visceral sensation.[33,34] It is not surprising that sleep disturbances have been characterized as an extrapyramidal symptom of IBS, based on the high prevalence of patients who subjectively report sleep disturbances and fatigue as among their most salient symptoms.[31,35] Interestingly, among individuals in the general population with self-reported sleep disturbances, IBS is also more prevalent,[27] underscoring the close relations between these central nervous system-mediated processes.

To our knowledge, 2 studies have explored the experience of sleep disturbance in patients with IBD. In the first study, patients with IBD endorsed that their sleep was poor, based on a single question in a broader QOL questionnaire.[27] A recent survey study from our own lab that used a validated sleep questionnaire to measure sleep complaints in patients with IBD, patients with IBS, and healthy controls suggested that patients with IBD self-reported significantly more difficulty with sleep initiation and maintenance, an increased likelihood of using sleeping aids, and more daytime impairment than did their healthy counterparts and were similar to patients with IBS on most measures.[36] We sought to expand on this line of inquiry, using validated questionnaires and polysomnography (PSG) to more precisely characterize sleep patterns in IBD.

METHODS

The study was approved by the Institutional Review Board at Rush University Medical Center. Participants were 16 patients with IBD (8 with Crohn's disease and 8 with ulcerative colitis), 9 patients with IBS, and 7 healthy subjects recruited through a university-based gastroenterology practice. All patients with IBD had inactive disease (based on classic endoscopic and histologic findings: Crohn's disease activity index < 150 and ulcerative colitis activity index < 3) to avoid confounding of inflammatory markers with sleep parameters, as nocturnal symptoms are commonly seen in patients with IBD when disease is active.

Diagnosis of IBS was based on Rome II criteria.[33] Healthy subjects were recruited through advertisement and had no intestinal symptoms or sleep concerns. Participants were excluded if they had already been diagnosed with a sleep disorder; had an altered sleep-wake cycle, such as shift work or delayed sleep phase syndrome; if they were taking antidepressant, anxiolytic, or hypnotic medication; if they were pregnant; or if they had another chronic medical condition (ie, congestive heart failure, history of stroke or brain injury, substance abuse) that would interfere with sleep parameters.

Patients with a Beck Depression Score-II greater than 14 or a State-Trait Anxiety Inventory[37] greater than 45 were also excluded to limit the effects of psychological disturbance on sleep parameters.[38,39] Mean (± SD) scores on the Beck Depression Inventory for the IBD, IBS, and healthy control groups were 8.5 ± 5.13, 12.86 ± 5.93, and 2.14 ± 2.91, respectively; both of the gastrointestinal groups significantly differed from the controls ($p = .05$, $p = .001$) but not from each other. Mean scores on the State-Trait Anxiety Inventory for the IBD, IBS, and healthy control groups were 40.40 ± 7.59, 43.00 ± 9.86, and 28.50 ± 10.11, respectively. Consistent with other literature, the IBS group significantly differed from controls in this regard ($p = .03$).

After signing consent, participants completed a demographic questionnaire and a series of validated questionnaires regarding their perception of their sleep and their general and disease-specific QOL.

The Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI)[40] is an 11-item self-report questionnaire that evaluates sleep quality and the nature of

sleep disturbances over the past month. This questionnaire yields 6 subscales referencing sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping aids, and daytime dysfunction. It also produces a global sleep score. The PSQI has been shown to be valid and reliable in discriminating good and poor sleepers and is closely associated with PSG parameters. We added 5 questions at the end of this questionnaire inquiring about the participants' perceived relations between sleep and gastrointestinal disease in the past month.

The Epworth Daytime Sleepiness Inventory

The Epworth Sleepiness Scale (ESS)[41] is an 8-item self-report questionnaire that has proved reliable for measuring daytime sleepiness in adults.

Health-Related QOL

The Health-Related QOL Questionnaire—Short Form-12v2[42] is a multipurpose short-form health-related QOL questionnaire based on the widely used SF-36 Health Survey.[43] Like the SF-36, this measure yields 2 scale scores—a physical component score and a mental component score. The SF-12 has been shown to be equally reliable and valid and more versatile than the alternative measure.[42]

IBD QOL

The IBD Quality of Life scale (IBDQ)[44] is a 32-item disease-specific questionnaire used to assess health-related QOL in participants with IBD. The questionnaire has 4 domains, including bowel symptoms, systemic symptoms, emotional factors, and social factors. Participants rate, on a 7-point Likert scale ranging from 1 (worst of health) to 7 (best of health), a variety of symptoms and concerns. Scores range from 32 to 224, with higher scores representing better health. When compared with healthy controls, participants with IBD report significantly impaired QOL across all 4 domains.[45,46] Typically, scores on the IBDQ correspond with disease activity[47] and, therefore, serve as a useful marker of symptom severity.

After completing questionnaires, participants were scheduled for nocturnal PSG. They were instructed to arrive at the Rush Sleep Disorders Center at 8:00 PM the night of their study and to maintain their typical bedtime. All participants were required to be in bed for 8 hours to ensure that time in bed was held constant. Nocturnal sleep recordings were completed using standard placement of electrodes for continuous monitoring of the central and occipital electroencephalograms (scalp sites C3, C4, O1, and O2 referenced to contralateral mastoid leads), electrooculogram, submental electromyogram, electrogastrogram, and 2 chest leads for cardiac rhythm. Additionally, respiration was measured with nasal and oral thermistors, thoracic and abdominal respiratory effort belts, and finger pulse oximetry. Bilateral leg (anterior tibialis) and arm movements (dorsal forearm) were monitored by surface electromyogram leads. Sleep recordings were collected using Sandman digital acquisition systems (Tyco, Ottawa, Canada). The low-frequency filter was set at 0.3 Hz and the high-frequency filter was set at 30 Hz, with sensitivity at 5 μV per millimeter for the electroencephalogram and electrooculogram. The electromyogram low- and high-frequency filters were set at 10 Hz and 63 Hz, with a sensitivity of 1 μV per millimeter. All electrode impedances were required to be less than 10 kΩ (5 kΩ for scalp electroencephalogram and mastoid leads). Each PSG recording was scored manually in 30-second epochs according to standard criteria. Arousals were scored according to standard criteria.

After PSG, participants were also asked to monitor their sleep prospectively for 1 week to corroborate self-report sleep measures. Data was corroborated through simultaneous wrist actigraphy. The Rush Sleep Diary is based on current recommendations for self-monitoring of sleep parameters and includes the following variables: presence of unusual stressors, alcohol or sleeping medications, time to bed, sleep onset latency, number of awakenings and amount of time awake, wake-up time, total sleep time, subjective feeling of being rested, daytime sleepiness rating, daytime fatigue rating, whether napping occurred, and the amount of time spent napping.[48] Given the complexity of these data, results will be reported elsewhere.

RESULTS

Demographic data are reported in Table 1. The mean age of the IBD group was 41.44 ± 13.31 years; the mean age of the IBS group was 52.67 ± 12.12 years. The IBD and IBS groups did not differ with respect to age, but the healthy controls were significantly younger than the IBS group (34.29 ± 9.39); thus, we controlled for age in subsequent analyses. Average duration of disease was 5.78 ± 9.20 years for the patients with IBS and 9.86 ± 10.17 years for the IBD group; this was not significantly different. Healthy controls were slightly more educated than the groups with gastrointestinal disorders; education is not known to affect sleep parameters, so we did not control for this in subsequent analyses. There were no differences between groups regarding marital status or ethnicity. The sample was 81% white, 63% married, and 60% female.

Subjective Reports of Sleep

Multivariate analyses of variance with posthoc tests were performed for the 3 disease groups for the subjective sleep ques-

Table 1—Demographic Variables

Disease group	Age, y	Women, %	Married, %	White, %	Disease duration, y	Education, y
IBD (n = 16)	41.44 ± 13.31	56	63	94	9.86 ± 10.17	15.13 ± 3.24[a]
IBS (n = 9)	52.67 ± 12.12[b]	78	67	78	5.78 ± 9.20	14.89 ± 3.44[b]
Control (n = 7)	34.00 ± 9.61[b]	43	57	57	—	19.86 ± 2.03[ab]
Total (N = 32)	42.97 ± 13.72	60	63	81	8.70 ± 9.93	16.09 ± 3.61

Data are presented as mean ± SD unless otherwise indicated. IBD refers to inflammatory bowel disease; IBS, irritable bowel syndrome.
[a]Groups that share this superscript significantly differ, $p < .05$
[b]Groups that share this superscript significantly differ, $p < .05$

Table 2—Results of the Pittsburgh Sleep Quality Index by Disease Category

Sleep Parameter	IBD (n = 16)	IBS (n = 9)	Controls (n = 7)	$F_{2,26}$	P value
Component 1: sleep quality	1.36 ± .63[a]	1.88 ± .84[b]	0.29 ± .49[ab]	11.05	.00[c]
Component 2: sleep latency	1.29 ± 1.07	1.63 ± 1.30	0.57 ± 1.13	1.63	.22
Component 3: sleep duration	1.14 ± .77	1.75 ± .71[b]	0.57 ± .53[b]	5.24	.01[c]
Component 4: habitual sleep Efficiency	0.79 ± 1.12	1.50 ± 1.20[b]	0 ± 0[b]	4.14	.03[c]
Component 5: sleep disturbances	1.36 ± .63	2.00 ± .76[b]	0.86 ± .69[b]	5.35	.01[c]
Component 6: use of sleeping medications	1.21 ± 1.25	1.63 ± 1.41	0.14 ± .38	3.25	.06
Component 7: daytime dysfunction	1.86 ± 1.40	2.88 ± 2.17	1.14 ± 1.21	2.22	.13
PSQI global score	9.00 ± 4.84[a]	13.25 ± 4.83[b]	6.71 ± 2.23[ab]	9.05	.00[c]
ESS score	8.09 ± 5.17	10.00 ± 6.7	6.71 ± 2.23	.70	.51
Naps in past month, no.	5.71 ± 8.2	2.25 ± 2.87	0 ± 0	2.30	.12

Data are presented as mean ± SD unless otherwise indicated. IBD refers to inflammatory bowel disease; IBS, irritable bowel syndrome; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale.
[a]Groups that share this superscript significantly differ, $p < .05$
[b]Groups that share this superscript significantly differ, $p < .05$
[c]Significant differences noted, $p < .05$

tionnaires, including the PSQI and ESS. Given age differences between groups at baseline, we also included age as a factor in the multivariate analyses of variance to determine possible interaction or main effects of age. There were no main ($F = 1.45$, $p = .27$) or interaction ($F = .80$, $p = .62$) effects of age noted. The IBS and IBD groups did not differ from each other on any of the subjective sleep components (1-7) of the PSQI. However, consistent with previous literature, IBS patients did indicate significantly poorer sleep quality, duration, and sleep efficiency and more sleep disturbances than the healthy controls.[32] In contrast, patients with IBD only reported poorer sleep quality when compared with healthy controls. Both the IBD and IBS groups had significantly higher PSQI global scores than healthy controls. The 3 groups did not differ with respect to sleep-onset latency, daytime dysfunction, or daytime sleepiness (ESS). There was a numeric trend such that the gastrointestinal groups reported more-frequent use of sleeping medication when compared with healthy controls ($p = .06$); they did not differ from each other. (Table 2).

In addition to using the validated measures of sleep perception and daytime sleepiness, we also inquired about perceived links between sleep and gastrointestinal symptoms in our IBS and IBD samples using nonparametric (χ^2) tests. Interestingly, the IBS group was more likely to endorse the statement "my intestinal symptoms make it difficult for me to go to sleep" than did the IBD group, and there was a numeric trend for the IBS group to be more likely to endorse the statement "my intestinal symptoms make me uncomfortable at bedtime." Results are presented in Table 3.

Objective Sleep Parameters

Multivariate analyses of variance with posthoc tests were performed for the 3 disease groups for the objective sleep parameters obtained by PSG. Given age differences between groups at baseline, we included age as a factor in the multivariate analyses of variance to determine possible main or interaction of age. There were no main ($F = 1.27$, $p = .17$) or interaction ($F = 2.84$, $p = .06$) effects of age noted. Specifically, we were interested in (1) total sleep time, (2) sleep efficiency; (3) sleep-onset latency, (4) percentage of stage 1 sleep, (5) percentage of stage 2 sleep, (6) percentage of SWS, (7) percentage of REM sleep, (8) latency to REM sleep, (9) the overall arousal index, (10) the apnea-hypopnea index, and (11) the periodic limb movement with arousal index (Table 4). Again, similar to subjective report, there were no significant differences between the IBD and IBS groups on any of the objective sleep parameters. However, patients with IBS did exhibit significantly less total sleep time and reduced sleep efficiency when compared with controls. Numerically, the IBD group fell in between the IBS and control groups on most parameters. There were also several numeric and clinically significant differences between the gastrointestinal groups and healthy controls with respect to percentage of stage 1 sleep and the overall arousal index, including the apnea-hypopnea index and the periodic limb movement index, reinforcing the presence of disrupted sleep in patients with IBD and IBS.

Interestingly, 4 participants (13%) were diagnosed with clinically significant sleep apnea (1 central, 3 obstructive). Three of these participants were in the IBD group, and 1 participant had IBS. These participants were kept in the final analyses because their presence did not alter the overall results.

Correlations Between Subjective and Objective Parameters

We performed bivariate correlations between the PSQI components and the associated PSG parameter for the IBD and IBS groups. PSG sleep efficiency was significantly correlated with its PSQI component 4 score, habitual sleep efficiency ($r = -.42$, $p = .03$). Self-reported hours of sleep per night were significantly correlated with PSG total sleep time ($r = -.41$, $p = .03$). Sleep-onset latency and sleep disruptions between PSQI and PSG were not significantly correlated. These findings should be interpreted with caution because age was significantly correlated with arousal index on PSG ($r = .48$, $p = .02$). Age was not correlated with any other variables.

Relations Between Sleep and QOL

Of note, our patients had poor QOL at baseline, in spite of being in remission. This could be due to their bowel symptoms or other concerns, including poor sleep. Although the constructs measured in the IBDQ and PSQI do not significantly overlap, linear regression analyses indicated that the PSQI global score accounted for as much as 60% of the variance in the IBDQ ($R^2 = .63$, $\beta = -4.39$, $t = -5.56$, $p = .001$), suggesting that perception of sleep is highly associated with disease-specific QOL. None of the PSG parameters were significantly associated with IBDQ;

Table 3—Perceived Relationships Between Sleep and Intestinal Symptoms

Question	IBD (n =16)		IBS (n =9)		χ^2	p value
	Yes	No	Yes	No		
Gastrointestinal symptoms lead to poor sleep	6, 43%	8, 57%	6, 75%	2, 25%	1.68	.20
"My intestinal symptoms wake me up"	5, 36%	9, 64%	6, 75%	2, 25%	3.14	.18
"My intestinal symptoms make it difficult for me to fall asleep"	1, 7%	13, 93%	6, 75%	2, 25%	10.80	.00[a]
"I have an urge to use the bathroom during sleep"	7, 50%	7, 50%	4, 50%	4, 50%	.09	1.0
"My intestinal symptoms cause me to worry at bedtime"	6, 43%	8, 57%	6, 75%	2, 25%	2.12	.16
"My intestinal symptoms make me uncomfortable at bedtime"	3, 21%	11, 79%	5, 63%	3, 38%	3.71	.08
Poor sleep leads to intestinal symptoms	9, 64%	5, 36%	6, 75%	2, 25%	.55	.62
"During a flare-up, my sleep is poor"	7, 50%	7, 50%	6, 75%	2, 25%	1.32	.38
"Poor sleep increases intestinal symptoms the next day"	6, 43%	8, 57%	4, 50%	4, 50%	.91	.63
"Poor sleep makes it harder to cope with symptoms"	8, 57%	6, 43%	6, 75%	2, 25%	2.30	.32
"Chronic poor sleep can cause a flare-up of my disease"	5, 36%	9, 64%	4, 50%	4, 50%	1.12	.58

IBD refers to inflammatory bowel disease; IBS, irritable bowel syndrome.
[a]Significant differences noted, $p < .05$

however, it is unlikely that any single night's sleep (especially in a research lab environment) would be predictive of disease-specific QOL, which references a time period of 2 weeks. Age was not a predictor in this model ($t = -.16$, $p = .87$).

With respect to general health-related QOL, as measured by the SF-12v2 in the entire sample, scores on the PSQI accounted for as much as 25% of the variance of the physical component score ($R^2 = .25$, $\beta = -.05$, $t = -2.91$, $p = .01$) and as much as 43% of the variance of the mental component score ($R^2 = .43$, $\beta = -.08$, $t = -4.36$, $p = .00$). Age was not a predictor in either the physical component score model ($t = -1.19$, $p = .25$) or the mental component score model ($t = 1.54$, $p = .14$). Finally, variables obtained from the prospective diary ratings were also independently predictive of the mental component score [$R^2 = .65$, $F = 6.53$, $p = .00$] but not physical component score. Again, none of the PSG parameters were significantly associated with either the mental or physical component score.

DISCUSSION

This study is the first to comprehensively report on sleep parameters, subjectively and objectively, in patients with IBD. This study was also unique in that patients with IBS served as a non-inflammatory control group, and both groups were compared with healthy subjects. There was considerable support for the perception of sleep disruption in patients with inactive IBD when compared with healthy controls and minimal differences between IBD and IBS patients on any subjective parameters. As has already been suggested in IBS,[27] sleep disturbances may also be an extrapyramidal symptom of IBD. Patients with IBD reported significantly poorer sleep quality and higher PSQI global scores than did healthy controls. When compared with healthy subjects, the IBS group additionally differed on the PSQI with respect to self-reported sleep efficiency, duration of sleep, and presence of disturbances.

The PSQI global score accounted for as much as 60% of the variance in the IBD QOL scale, underscoring the need to address sleep concerns in the management of IBD. Although our population was in remission from their disease, they still reported impaired QOL and reduced sleep quality. This could be expected given the impact of disease activity on both QOL and sleep—although the disease may not necessarily be in "flare," symptoms can still be present, supporting the notion that disturbed sleep quality may be a lingering symptom of flare that does not fully recover in between.

Although links between the PSQI and general health-related QOL (SF-12) were not as robust or consistent, QOL, particularly mental health QOL, was still significantly impacted by sleep concerns. Finally, as many as 43% of our patients with IBD reported that gastrointestinal symptoms led to poor sleep, and 64% of patients with IBS indicated that poor sleep led to intestinal symptoms.

Although the IBD group resembled the IBS population on most parameters, the IBS group often numerically scored the highest on markers of distress. This is consistent with other literature that suggests that patients with IBS may have heightened awareness of bodily sensations and may be more likely to report symptoms than are patients with other gastrointestinal disorders.[49,50] IBS is also a disorder of heightened arousal—there is recent evidence indicating that such chronic autonomic hyperarousal may explain the observed links between sleep loss and coronary events[51] and may be a second pathway contributing to medical morbidity in a host of diseases.

On PSG, the IBD group did not differ from either IBS or healthy control groups on any parameter and consistently fell numerically between IBS and controls. Consistent with prior research, the IBS group additionally evidenced significantly less total sleep time and reduced sleep efficiency when compared with healthy controls.[32] Again, hyperarousal and difficulty accommodating new environments, which are commonly associated with IBS[34] and are not as salient in IBD, may explain these findings

In earlier research, patients with IBS undergoing PSG and actigraphy have exhibited reduced amounts of SWS and significantly more sleep fragmentation than healthy controls, even after controlling for the frequently comorbid psychiatric disturbances, such as depression and anxiety.[32] Although not seen in this study, an increased proportion of REM sleep (but not number of REM episodes) has also been reported in patients with IBS when compared with healthy controls.[29] There is also evidence that, in normal individuals, REM sleep, arousals, and morning awakening have immediate stimulatory effects on colonic motility[21]; fragmented sleep patterns seen in patients with hyperresponsive in-

Table 4—Objective Sleep Parameters by Disease Category

Sleep Parameter	IBD (n = 16)	IBS (n = 9)	Controls (n = 7)	$F_{2,26}$	p value
Total sleep time, min	418.55 ± 55.67	365.65 ± 66.44[a]	464.18 ± 19.26[a]	5.49	.01[b]
Sleep efficiency, %	84.44 ± 5.06	78.0 ± 13.43[a]	92.76 ± 4.73[a]	5.05	.01[b]
Sleep-onset latency, min	20.86 ± 17.99	20.34 ± 29.20	18.80 ± 29.77	.02	.99
Sleep stage, %					
1	12.38 ± 5.21	14.03 ± 9.14	6.46 ± 5.11	2.22	.13
2	50.32 ± 10.34	48.93 ± 12.32	53.48 ± 3.71	.31	.74
SWS	16.54 ± 8.41	15.60 ± 8.51	14.80 ± 8.87	.09	.91
REM	20.73 ± 5.24	21.43 ± 7.27	25.24 ± 2.36	1.23	.30
Latency to REM, min.	125.50 ± 61.52	115.65 ± 58.36	105.30 ± 30.90	.26	.77
Overall arousal index, no./h	17.89 ± 12.10	18.73 ± 10.56	8.70 ± 3.55	1.29	.29
Apnea-hypopnea index, no./h	8.70 ± 14.90	7.45 ± 9.14	.43 ± .50	.70	.51
Periodic leg movement, w/arousal index no./h	4.35 ± 6.89	3.35 ± 5.22	1.42 ± 1.28	.48	.63

Data are presented as mean ± SD. IBD refers to inflammatory bowel disease; IBS, irritable bowel syndrome; SWS, slow-wave sleep; REM, rapid eye movement sleep.

[a]Groups that share this superscript significantly differ, $p < .05$.

[b]Significant differences noted, $p < .05$.

testinal tracts (as is the case with both IBD and IBS) may enhance or promote alterations in colonic motility.

Both the IBD and IBS groups in this study had mean sleep efficiencies under 85% and almost twice the amount of stage 1 sleep and arousal indexes (17.89 and 18.73, respectively) when compared with controls. These findings are consistent with self-reports in both the IBD and IBS groups, who indicated markedly reduced sleep quality, compared with controls, and a greater number of sleep disturbances. Patients with IBS reported the most daytime sleepiness on the ESS, followed by patients with IBD, followed by controls; this finding was not statistically significant between the gastrointestinal groups in this study. Although patients with IBS reported the most sleepiness, patients with IBD reported taking almost twice the number of naps per month as the IBS group and 5 times the number of naps of controls. Research on patients with insomnia suggests that patients with primary insomnia have difficulty napping during the day, despite decreased total sleep time at night and regardless of self-reported sleepiness, likely due to a state of persistent hyperarousal.[52] We speculate that our IBS group, another group with persistent hyperarousal, could share this feature with patients with insomnia. On the other hand, patients with IBD, a group that does not typically manifest hyperarousal, is able to nap during the day and may share features with other more truly "sleepy," patient populations, such as those with periodic limb movement disorder or obstructive sleep apnea.[53] Quantifying daytime sleepiness with multiple sleep latency tests may ultimately be an important direction toward differentiating initiating and maintaining factors of sleep disturbance in both groups.

Because sleep has not been previously studied in IBD, consistent patterns of sleep disturbance in this population remain to be identified. Comparison of patients with active and inactive IBD and continued comparisons between IBS and IBD groups may provide additional insight into the pathogenesis and impact of sleep disturbance in both groups. Although the design of this study does not allow for speculation regarding the pathogenesis of sleep disturbances in these groups, altered immune function, systemic inflammation (such as cytokines), or a combination thereof could potentially play a role in the development of sleep disorders in IBD. It has been fairly well established that altered immune function and low-grade inflammatory process are present in patients with IBD,[26] and proinflammatory cytokines such as IL-6 have been linked to altered sleep.[11] Sleep disorders can also arise as a result of autonomic arousal, psychopathology, heightened stress, or stress-initiated central nervous system activity.[54] These latter processes are likely more relevant to IBS, a disorder characterized by chronic hyperarousal and altered central nervous system activity.[34]

Although IBS and IBD patients may resemble each other on PSG and self-report data with respect to sleep disturbances, the factors maintaining sleep disturbances in both populations may not be the same as the factors that initiate such disturbances. Sleep problems that begin before or during an IBD disease flare secondary to immune and inflammatory processes may be maintained when the patient is in remission by conditioned insomnia, continued low-grade abdominal pain or diarrhea, worry about future flares, or other psychosocial consequences associated with having IBD. Prospective monitoring of sleep in IBD is another important direction for future research.

Our data demonstrating disrupted sleep in patients with IBD in remission has important clinical implications. Current treatments for IBD are aimed at attenuating the inflammatory response once a flare has occurred and include corticosteroids, sulfasalazine, and 5-aminosalicylate compounds; these medications have significant side effects, have poor adherence,[55] and are only effective in a portion of patients.[56] Regardless of whether disrupted sleep in patients with IBD is a primary or secondary event, its potential deleterious effects to initiate disease flare-up would be the same. If sleep disturbance contributes to the initiation of the inflammatory process, therapy directed at improving sleep during a flare could potentially attenuate the inflammatory cascade and induce remission. Alternatively, long-term therapy of disrupted sleep could potentially prevent the initial activation of the mucosal immunoinflammatory response and either reduce the risk of flare-up or extend the periods of remission. Further studies are needed to determine the effects of therapeutic intervention for disrupted sleep on the course of IBD.

The study is possibly limited by small sample size, age differences between the control group and the gastrointestinal groups, and the possibility of a first-night effect.

CONCLUSION

This study supports the presence of sleep concerns in patients with IBD. Indeed, patients with IBD did not seem to significantly differ subjectively from patients with IBS, a group for whom sleep complaints have been established as an extrapyramidal symptom. On PSG, total sleep time differentiated the 3 groups well, with the IBS and IBD groups appearing numerically similar on most parameters. Although the IBS and IBD groups were similar in most regards, patients with IBS did consistently report the most concerns. Sleep parameters greatly influenced both disease-specific and general health-related QOL in both groups and highlight the need to address sleep concerns as part of IBD management.

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