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The Effect of Dream Anxiety on Sleep Quality in Inflammatory Bowel Diseases

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Keywords
Anxiety · Crohn's disease · Depression · Dream anxiety · Inflammatory bowel disease · Ulcerative colitis

Abstract
Introduction: Declining sleep quality is a well-known issue in inflammatory bowel disease (IBD), but dream characteristics of patients with IBD and their role in sleep quality are unknown. In this study, we aimed to examine whether and how patients with ulcerative colitis (UC) and Crohn's disease (CD) differ on sleep quality, sleepiness level, and dream anxiety (DA) level compared to healthy controls (HC), controlling for their depressive and anxious tendencies. ***Methods:*** Patients and HCs were enrolled prospectively into the study. The Van DA Scale, Pittsburg Sleep Quality Index, Epworth Sleepiness Scale, Beck Depression Index, and State-Trait Anxiety Inventories were used to assess DA, sleep quality, sleepiness, depression, and anxiety, respectively. ***Results:*** Patients with IBD had significantly lower depression (p = 0.004), state anxiety (p = 0.0001), trait anxiety (p = 0.004), and DA (p = 0.0001) than HCs. Although no statistically significant difference in sleep quality was found (p = 0.99), daytime sleepiness was more common in HCs than in IBD patients (p = 0.0001). No statistically significant difference was seen in depression, state anxiety, trait anxiety, DA, sleep quality, and daytime sleepiness between patients with CD and those with UC. No correlation was found between disease activity indices and psychological parameters. ***Conclusion:*** In contrast to previous studies, this study found lower anxiety and depression levels in patients with IBD than in HCs. Moreover, DA score was higher in HCs. For the first time, we revealed that DA may be one of the factors leading to sleep disturbance in patients with IBD.
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Introduction

Inflammatory bowel diseases (IBDs), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic, idiopathic, inflammatory diseases of the gastrointestinal tract [1]. Sleep is a complicated condition that is still not clearly understood. Several chronic inflammatory and immune disorders, such as systemic lupus erythematosus and rheumatoid arthritis, can affect sleep quality [2, 3]. This relationship was also seen between IBD and sleep quality [4]. Sleep disturbance may be seen in patients with IBD, but the reasons are still unclear. IBD may affect sleep quality as a result of activated inflamma-

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tory cytokines. Beside this, disease activity and sleep disturbances were also found to be correlated [5].

Nightmares are dreams that cause threat, anxiety, or fearful feelings and always occur in rapid eye movement sleep [6]. Dream anxiety (DA) is defined as frightening dreams that cause people to wake up, and after awakening, they fully remember the dream. Nightmares differ from DA because they do not cause sudden awakening during sleep [7]. DA is accepted as clinically significant if it occurs at least one time in a week; however, 85% of adults report experiencing DA at least once a year [8]. In large population studies, clinically significant DA was seen in 0.9–6.8% of healthy people [9, 10]. Psychological conditions such as depression, anxiety, and schizophrenia can cause DA [11–13]. In addition, DA is more common in people with depression, anxiety, and sleep disorders [14, 15]. Neurocognitive treatment of DA was shown to decrease depression and anxiety, thus suggesting a bidirectional relationship between DA, depression, and anxiety [16].

Complicated relationships exist between depression, anxiety, and sleep disturbances, all of which are commonly seen in IBD. Although the literature shows a body of evidence on the impaired sleep quality of patients with IBD, information about the factors that cause deterioration in sleep quality is insufficient. Therefore, in this study, we aimed to investigate the levels of DA, depression, anxiety, sleep quality, and sleepiness in patients with IBD and evaluate the relationship between DA and sleep quality. Our first hypothesis was that DA is high in IBD patients and is associated with low sleep quality and high sleepiness, and our second hypothesis was that high DA and impaired sleep quality are related to the severity of the disease.

Materials and Methods

Participants

The study consisted of 304 participants. Patients who enrolled in the study had a follow-up visit after an IBD diagnosis in our IBD-specific gastroenterology outpatient clinic from November 2016 to January 2017. IBD diagnosis was established with clinical, biochemical, endoscopic, and histological findings according to the current European Crohn's and Colitis Organization's guidelines at the time of the diagnosis. Detailed information about the study was given to the patients. For patient and healthy control (HC) groups, the exclusion criteria were illiteracy, intellectual disability, a history of any psychiatric diagnosis or current psychotropic agent usage, a history of any neurological disease that may interfere with sleep, sleep apnea, pregnancy, or working on a night shift schedule. In total, 136 patients who met the participation criteria were prospectively enrolled into the study. The HC group consisted of healthy relatives of patients who followed up at other outpatient clinics in our hospital.

Assessments

The Beck depression inventory (BDI) is a self-report questionnaire that measures the risk and level of depression [17]. It includes a total of 21 questions and each question is rated on a Likert scale ranging from 0 to 3. Total scores range from 0 and 63. The higher scores represent higher risk and severity of depression. BDI's validity and reliability have been previously established [18].

The State-Trait Anxiety Inventory is a self-report scale that measures state and trait anxiety levels with 20 questions for each [19]. State anxiety measures the person's anxiety in current time and condition. Trait anxiety measures the person's chronic anxiety, independent from any time or condition. Each question is rated on a Likert-type scale ranging from 1 to 4. The scale scores range from 20 to 80, and higher scores reflect higher state and trait anxiety. This scale has high validity and reliability coefficients [20].

The Epworth Sleepiness Scale (ESS) contains 8 self-report questions that are rated on a 4-point Likert scale ranging from 0 to 3. It measures the sleepiness of the person in the daytime, and higher scores reflect higher levels of sleepiness [21]. The ESS's validity and reliability have been previously established [22].

The Pittsburg Sleep Quality Index (PSQI) measures the sleep duration, quality, and presence of a sleeping disorder over 1 month. This questionnaire includes 24 questions. The participant answers 19 questions, and the sleeping partner of the participant answers 5 questions. Total scores range from 0 to 21, and higher scores correspond with poorer sleep quality. A score >5 indicates poor sleep quality [23, 24].

The Van DA Scale (VDAS) consists of 17 questions rated on a 5-point Likert scale (0–5). It measures nightmare frequency and the anxiety that arises from dreams. It also evaluates the relationship between the person's dreams and their effects on him/her [25]. Higher scores show a higher aversive effect of dreams on the person.

Medical characteristics of the patients were assessed by the following indicators. The first indicator was blood test results, including hemoglobin (g/dL), mean platelet volume (fL), albumin (g/dL), C-reactive protein, and sedimentation (mm). Second, the CD activity index was used to assess the activity level of patients with CD [26]. The CD activity index is composed of 8 questions and also asks about hematocrit levels. A score ≤150 indicates inactive disease. A score above 150 indicates active disease, while a score >450 shows severe disease. Third, the Partial Mayo Score was used to determine UC disease activity [27]. It includes stool frequency, rectal bleeding, and physician's global assessment. The score ranges from 0 to 9: 0–2 indicates inactive disease; 3–4, mild disease; 5–6, moderate disease; and 7–9, severe disease. Lastly, we assessed disease involvement based on the Montreal classification [28].

The sociodemographic characteristics of the participants were assessed with a form that was developed in our outpatient clinic. The form includes questions about gender, age (years), education level (years), marital status (single or married), number of children, employment status (yes: working; no: not working), job tenure (<5 years, >5 years), and occupation (civil servant/worker or self-employed). It also calculates the body mass index (kg/m^2) of all participants.

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Data Collection Procedure

All participants gave written informed consent prior to participating in the study. For all patients, a detailed anamnesis was taken, and a complete physical examination was performed. Physician-assessed sociodemographic data (age, gender, etc.), IBD characteristics (disease activity, type, duration, etc.), disease involvement according to the Montreal classification [28], and blood test results recorded at the time of examination. All enrolled participants completed self-report questionnaires (BDI, State-Trait Anxiety Inventory, ESS, PSQI, and VDAS) under physician supervision. Sociodemographic data of HCs were recorded by the physician, and HCs filled the self-report scales under a physician supervision. All participants were also free to ask questions about the questionnaires.

Statistical Analyses

The descriptive statistics included frequencies, percentages, means, and SDs. We conducted a chi-square analysis and one-way analysis of variance to compare sociodemographic and medical characteristics by group. The comparison of disease location of patients according to Montreal classification, we used nonparametric version of analysis of variance, Kruskal-Wallis test. Pearson correlations were conducted to examine the interrelations among scale variables. A multivariate analysis of variance with covariates (MANCOVA) was performed to test group differences on sleep indicators, controlling for depression, anxiety, and sociodemographic characteristics. We utilized Tukey's D for post hoc comparisons. Finally, a multiple regression analysis was used to test the predictors of sleep quality among patient groups versus HCs. Significance was defined as a p value <0.05.

Results

Participant Baseline Characteristics

Table 1a presents descriptive statistics of each group. Table 1b shows the comparison of sociodemographic characteristics by groups. Groups significantly differed by age ($p < 0.05$), education level ($p < 0.01$), and the number of children ($p < 0.01$). The HC group was significantly younger than the UC group (mean difference, –5.17 ± 1.98; $p < 0.05$) and had fewer children than the CD group (mean difference, –0.98 ± 0.18; $p < 0.001$) and the UC group (mean difference, –1.04 ± 0.21; $p < 0.001$). The HC group had a higher education level than the CD (mean difference, 4.73 ± 0.65; $p < 0.001$) and UC groups (mean difference, 3.31 ± 0.67; $p < 0.001$). Groups only significantly differed by marital status (χ^2 [2], 20.01; $p < 0.001$). Groups did not significantly differ on gender, employment status, work tenure, or employment type (Table 1b).

Table 1b also illustrates the univariate comparisons of medical characteristics of the patient groups. No significant group difference was seen in body mass index, years since first diagnosis of IBD, number of attacks since the first diagnosis, or any biochemical indicators.

Table 2 shows the means and SDs of scale scores by study groups. Sociodemographic characteristics were not significantly related to sleep quality or sleepiness. In contrast, DA was higher for participants who were married ($r = 0.22$; $p < 0.01$), younger ($r = 0.13$; $p < 0.05$), and had fewer number of children ($r = –0.19$; $p <0.05$). We compared DA, sleep quality, and sleepiness levels of patient subgroups according to the Montreal classification. Kruskal-Wallis tests indicated that there were no significant subgroup differences on DA (H = 1.11, $p = 0.58$ for CD group; H = 0.68, $p = 0.71$ for UC group), sleep quality (H = 0.80, $p = 0.67$ for CD group; H = 2.81, $p = 0.25$ for UC group), or sleepiness (H = 2.54, $p = 0.28$ for CD group; H = 0.39, $p = 0.82$ for UC group) for each patient group.

In summary, we found group differences in age, marital status, education level, and the number of children among the study groups. These sociodemographic variables can interfere with sleep quality, sleepiness, or DA. Significant correlations among DA and marital status, age, and the number of children support such potential interference. Therefore, these group differences in sociodemographic data can potentially confound further analyses. Group differences on sleep- and dream-related variables may be attributed to differences in sociodemographic data rather than being healthy or having IBD. To avoid such confounding effects, we controlled these variables in subsequent multivariate group comparisons.

Correlations among Sleep Quality, DA, Sleepiness, Depression, and Anxiety

According to the Pearson correlations presented in Table 3, poor sleep quality was significantly associated with higher depression ($r = 0.54$; $p < 0.01$) and anxiety levels ($r = 0.15$, $p < 0.05$). Sleepiness had a significant positive correlation with depression ($r = 0.42$; $p < 0.01$) and anxiety ($r = 0.19$; $p < 0.01$). Like sleep quality and sleepiness, DA was significantly related to higher depression ($r = 0.64$; $p < 0.01$) and anxiety levels ($r = 0.28$; $p < 0.05$). In summary, depression and trait anxiety levels were related to poorer sleep quality, higher DA, and higher sleepiness for all participants. Analyses also suggest that sleep quality is positively related with DA ($r = 0.58$; $p < 0.01$) and sleepiness ($r = 0.36$; $p < 0.01$).

Comparison of Study Groups by Sleep Quality, DA, and Sleepiness

Table 4a and b present the results of the MANCOVA, in which we compared study groups (HCs, CD group, UC group) by sleep quality, DA, and sleepiness. Covariates were sociodemographic data (age, education, number of

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Table 1.

a Participant baseline characteristics by group

	HCs (*n* = 168), mean ± SD	All patients (*n* = 136), mean ± SD	CD (*n* = 72), mean ± SD	UC (*n* = 64), mean ± SD
Age, years	36.54±14.15	39.28±12.75	37.13±12.04	41.70±13.19
Education, years	14.05±4.79	9.99±4.35	9.32±4.24	10.73±4.38
Number of children	1.15±1.46	2.16±1.07	2.13±0.97	2.20±1.17
BMI, kg/m^2	24.84±4.73	25.04±4.30	24.67±4.68	25.47±3.82
Disease duration, years	N/A	5.74±4.56	5.33±4.04	6.20±5.08
Number of attacks	N/A	1.40±1.38	1.27±1.08	1.53±1.65
Hemoglobin, g/dL	N/A	13.52±1.77	13.37±2.02	13.68±1.46
Mean platelet volume, FL	N/A	8.35±1.06	8.27±0.83	8.42±1.27
Albumin, g/dL	N/A	4.48±0.49	4.43±0.55	4.53±0.43
C-reactive protein	N/A	4.64±6.46	4.20±4.38	5.11±8.24
Sedimentation, mm	N/A	21.32±17.17	25.09±20.56	17.55±12.26
Location of the disease according to montreal classification, *n* (%)				
Terminal ileum	N/A	N/A	23 (32.0)	N/A
Colon			8 (11.0)	
Ileocolon			39 (54.0)	
Upper GI			2 (3.0)	
Ulcerative proctitis	N/A	N/A	N/A	5 (8.0)
Left-sided colitis				33 (52.0)
Extensive colitis				26 (40.0)
Gender, *n* (%)				
Female	89 (53.0)	58 (42.6)	31 (43.1)	27 (42.2)
Male	79 (47.0)	78 (57.4)	41 (56.9)	37 (57.8)
Marital status, *n* (%)				
Single	75 (44.6)	95 (69.9)	48 (66.7)	47 (73.4)
Married	93 (55.4)	41 (30.1)	24 (33.3)	17 (26.6)
Employment status, *n* (%)				
Yes	84 (50.0)	72(52.9)	35 (48.6)	37 (51.4)
No	84 (50.0)	64(47.1)	37 (57.8)	27 (42.2)
Job tenure, years, *n* (%)				
>5	48 (39.7)	33(30.8)	20 (36.4)	13 (25.0)
<5	73 (60.3)	74 (69.2)	35 (63.6)	39 (75)
Occupation, *n* (%)				
Civil servant/worker	36 (43.4)	36 (39.1)	15 (31.2)	21 (47.7)
Self-employed/other	47 (56.6)	56 (60.9)	33 (68.8)	23 (52.3)

BMI, body mass index; N/A, not applicable; HC, healthy control; CD, Crohn's disease; UC, ulcerative colitis.

b Comparison of participant baseline characteristics

	Comparison of all patients with HCs		Comparison of 2 patient groups and HCs	
	F	df	F	df
Age, years	3.08	1	3.51*	2
Education, years	58.62**	1	31.14**	2
Number of children	33.90**	1	16.91**	2
BMI, kg/m^2	0.15	1	0.61	2
Disease duration, years	N/A		1.24	1
Number of attacks, *n*	N/A		1.18	1
Hemoglobin, g/dL	N/A		0.38	1
Mean platelet volume, FL	N/A		0.26	1
Albumin, g/dL	N/A		0.45	1
C-reactive protein	N/A		0.23	1
Sedimentation, mm	N/A		2.28	1

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Table 1 (continued)

	χ^2	df	χ^2	df
Gender	3.21	1	3.22	2
Marital status	19.38***	1	20.01**	2
Employment status	0.26	1	1.41	2
Job tenure	3.80	1	5.89	2
Occupation	35.70***	1	4.14	2

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
HC, healthy control; BMI, body mass index; N/A, not applicable.

Table 2. Results of 5 tested scales by study group

	HC group (n = 168), mean ± SD	All patients (n = 136), mean ± SD	CD (n = 72), mean ± SD	UC (n = 64), mean ± SD
PSQI	5.70±3.87	5.70±3.00	5.62±3.09	5.78±2.92
DA scale	10.23±10.06	5.42±7.48	5.96±7.96	4.84±6.94
ESS	6.99±4.39	3.14±2.65	3.14±2.68	3.14±2.63
BDI	13.24±11.66	10.05±7.54	9.71±7.25	10.42±7.88
STAI-trait scale	45.13±5.30	42.65±8.50	42.49±8.65	42.81±8.41

HC, healthy control; CD, Crohn's disease; UC, ulcerative colitis; PSQI, Pittsburgh Sleep Quality Index; DA, dream anxiety; ESS, Epworth Sleepiness Scale; BDI, Beck depression inventory; STAI, State-Trait Anxiety Inventory.

children), depression, and anxiety levels. The MANCOVA revealed significant multivariate effects for DA and sleepiness in relation to the study group after accounting for depression, trait anxiety, and sociodemographic variables. The multivariate effect was not significant for sleep quality.

Univariate analyses demonstrated that the UC group (4.84 ± 6.94) had a lower DA score than the CD group (5.96 ± 7.96); however, both groups had lower DA than the HC group (10.23 ± 10.06). Although the UC (3.14 ± 2.63) and CD groups (3.14 ± 2.68) did not significantly differ in sleepiness level, they had significantly lower sleepiness than the HC group (6.99 ± 4.39).

Comparison of Study Groups and Gender by Sleep Quality, Sleepiness, and DA

We further explored the multivariate interactive effect of marital status and study groups on sleep quality, sleepiness, and DA. However, no significant multivariate effect was found. To explore the interaction of gender and study

Table 3. The relationships between variables (Pearson correlation)

	PSQI	DA scale	ESS
PSQI	–	0.58**	0.36**
DA scale	–	–	0.46**
BDI	0.54**	0.64**	0.42**
Trait Anxiety Inventory	0.15*	0.28**	0.19*
Gender, male	0.03	–0.01	0.01
Marital status, married	0.08	0.22**	0.10
Age, years	–0.06	–0.13*	0.01
Education, years	–0.06	0.10	0.11
Number of children	–0.07	–0.19*	–0.08
Work tenure, years	–0.02	–0.09	–0.09

* $p < 0.05$.
** $p < 0.01$.
PSQI, Pittsburgh Sleep Quality Index; DA, dream anxiety; ESS, Epworth Sleepiness Scale; BDI, Beck depression inventory.

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Table 4.

a Results of MANCOVA: comparison of study groups (HCs, Crohn's group, UC group) on sleep quality, dream anxiety, and sleepiness, controlling for sociodemographic (age, education, number of children), depression, and anxiety

	Sleep quality			DA			Sleepiness		
	df	F	η^2	df	F	η^2	df	F	η^2
Study groups	2.00	1.63	0.01	2.00	3.22*	0.03	2.00	22.50**	0.15
Control variables									
Age, years	1.00	0.95	0.00	1.00	0.12	0.00	1.00	1.15	0.01
Education, years	1.00	1.29	0.01	1.00	0.11	0.00	1.00	0.26	0.00
Number of children	1.00	0.98	0.00	1.00	2.49	0.01	1.00	0.02	0.00
Depression	1.00	103.55**	0.29	1.00	162.00**	0.39	1.00	47.38**	0.16
Trait anxiety	1.00	0.95	0.00	1.00	3.19	0.01	1.00	0.02	0.00

* $p < 0.05$.
** $p < 0.01$.
MANCOVA, multivariate analysis of variance with covariates; UC, ulcerative colitis; HC, healthy control; DA, dream anxiety.

b Results of MANCOVA to compare patients with HCs on sleep quality, DA and sleepiness, controlling for sociodemographic (age, education, number of children), depression, and anxiety

	Sleep quality			DA			Sleepiness		
	df	F	η^2	df	F	η^2	df	F	η^2
Study groups	1.00	3.02	0.01	1.00	5.09*	0.02	1.00	43.68***	0.15
Control variables									
Age, years	1.00	1.63	0.01	1.00	0.51	0.00	1.00	1.34	0.01
Education, years	1.00	0.82	0.01	1.00	0.81	0.01	1.00	0.35	0.00
Number of children	1.00	0.14	0.00	1.00	1.11	0.01	1.00	0.01	0.00
Depression	1.00	103.34**	0.29	1.00	160.00**	0.39	1.00	47.31**	0.16
Trait anxiety	1.00	0.99	0.01	1.00	3.33	0.01	1.00	0.25	0.01

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
DA, dream anxiety; MANCOVA, multivariate analysis of variance with covariates; HC, healthy control.

groups, we conducted a 3 (study groups: HC, CD, and UC) × 2 (gender: female, male) MANCOVA on sleep quality, DA, and sleepiness, controlling for sociodemographic data (age, education, number of children), depression, and anxiety (Table 5). The multivariate effects of DA and sleepiness level were still significant in terms of study groups. In terms of gender group, the multivariate effect of DA was significant. The interaction of study group and gender was significant for sleep quality but not for DA or sleepiness.

Univariate analyses revealed that men (11.49 ± 10.28) had higher DA than women (9.10 ± 9.78). In terms of sleep quality, women in the CD group had significantly higher scores on the PSQI (7.32 ± 3.86), indicating worse sleep quality than men in the CD group (4.64 ± 1.59) and women in the HC group (4.89 ± 3.47). In contrast, we found no gender difference for UC group; female (6.50 ± 2.09) and male (5.40 ± 3.37) UC patients reported similar levels of sleep quality.

DA and Sleepiness as Predictors of Sleep Quality in Patient Groups versus HCs after Controlling for Depression and Trait Anxiety

We tested whether sleep quality was predicted by DA, sleepiness, and their interaction with the HC group versus patient groups, controlling for depression and trait anxiety levels. We conducted multiple linear regression analysis (Table 6). In the first step, we regressed depres-

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Table 5. Results of a 3 (study groups: HCs, Crohn's group, UC group) × 2 (gender: female, male) MANCOVA on sleep quality, DA, and sleepiness, controlling for sociodemographic variables (age, education, number of children), depression, and anxiety

	Sleep quality			Dream anxiety			Sleepiness		
	df	F	η^2	df	F	η^2	df	F	η^2
Study group	2.00	1.81	0.02	2.00	3.45*	0.03	2.00	22.56***	0.16
Gender	1.00	0.04	0.00	1.00	3.84*	0.02	1.00	1.79	0.01
Study group × gender	2.00	5.63**	0.04	2.00	0.21	0.01	2.00	0.32	0.01
Control variables									
Age, years	1.00	1.75	0.01	1.00	0.11	0.00	1.00	1.32	0.01
Education, years	1.00	0.86	0.00	1.00	0.25	0.00	1.00	0.37	0.00
Number of children	1.00	0.72	0.00	1.00	3.42	0.01	1.00	0.01	0.00
Depression	1.00	94.73	0.28	1.00	156.98	0.39	1.00	46.61***	0.16
Trait anxiety	1.00	0.09	0.00	1.00	5.57*	0.02	1.00	0.11	0.00

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
DA, dream anxiety; HC, healthy control; UC, ulcerative colitis; MANCOVA, multivariate analysis of variance with covariates.

Table 6. Moderating effect of group (patient group versus HCs) on the relationships between sleep quality, DA, and sleepiness, controlling for depression and trait anxiety

	B	SE B	β	R^2
Step 1				
Depression	0.553	0.051	0.556***	0.294***
Trait anxiety	−0.031	0.051	−0.031	
Step 2				
Depression	0.234	0.060	0.235	0.429***
Trait anxiety	−0.026	0.047	−0.026	
DA	0.508	0.076	0.509***	
Sleepiness	0.136	0.067	0.136*	
Group (patient group: 1; HCs: 0)	0.367	0.108	0.182*	
Group × DA	−0.280	0.107	−0.155*	
Group × sleepiness	0.003	0.124	0.001	

* $p < 0.05$.
*** $p < 0.001$.
HC, healthy control; DA, dream anxiety.

sion and trait anxiety on sleep quality. Two variables explained 29.4% variance in sleep quality. Depression significantly and positively predicted sleep quality score (β = 0.556; $p < 0.001$). In the second step, we added DA, sleepiness, patient groups versus HC group, and its interaction with other 2 variables (group × DA; group × sleepiness). All variables explained 42.9% of variance in sleep quality. DA (β = 0.509; $p < 0.001$) is the most important predictor of sleep quality, controlling for depression, anxiety, sleepiness and its interactive effects. Sleepiness also significantly predicts sleep quality (β = 0.136; $p < 0.05$). Both variables predict higher sleep quality score. Interaction analysis suggested that group and DA significantly interact to predict lower sleep quality score (β = –0.156; $p < 0.05$).

To understand the significant interaction between group and DA, we further plotted predicted values for the sleep quality. We chose groups at 1 SD below the mean (low value) and 1 SD above the mean (high value) of DA. The plot of our two-way interaction suggests that under the condition of low DA, patient groups scored higher on sleep quality when compared to HCs. Such a difference disappears when there is high DA.

Discussion

Sleep physiology and sleep-related disorders in IBD are only partially understood in the current literature. Past studies have revealed that sleep quality disturbance correlated with IBD severity and poor quality of life [29]. DA is one psychological entity that affects sleep quality. However, dream characteristics of patients with IBD and their effect on sleep have not been investigated before. In this study, we aimed to examine whether and how patients with IBD differ on sleep quality, sleepiness, and DA compared with HCs.

This study's main finding was that low DA is the most important predictor of sleep quality in IBD patients, after controlling for depression, anxiety, and sleepiness. High-

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er DA significantly predicts poorer sleep quality levels. Although the analyses revealed no significant main effect of group (patients vs. HCs), we found significant interactive effect between group and DA on sleep quality. That is, IBD patients who had low DA reported poorer sleep quality compared to HCs with low DA. This finding is very important because we found poorer sleep quality of IBD patients even though their anxiety and depression levels were lower than HCs. High DA levels seem to blur the significant difference between IBD patients and HCs on sleep quality. Our findings support previous studies which found that sleep quality is lower in patients with IBD than in healthy participants [30].

Moreover, we found a significant interactive effect for participant gender and study group on sleep quality. Women in the CD group had poorer sleep quality than men in the CD group and women in the HC group. This effect was still significant after controlling for factors that can be potentially detrimental for sleep quality in general, such as depression, anxiety level, sociodemographic characteristics such as age, education level, and the number of children. That is, irrespective of their depression or anxiety level, age, education, and number of children, women with CD had worse sleep quality. This finding is in line with studies that show poorer sleep quality in women than in men [31, 32]. Yet, it contradicts with a previous study, in which sleep quality was worse in female patients with UC compared to males with UC, and there was no significant gender difference between patients with CD [4]. This contradiction may be seen due to the differences in sample characteristics. Disease activity is associated with poor sleep quality, and different disease characteristics and activities between the 2 studies may contribute to this variation [33].

In terms of DA, we found significant differences between UC and CD groups. DA was significantly higher in the UC group than the CD group in multivariate analyses. In other words, accounting for depression, anxiety, and sociodemographic data of patients, as well as considering their sleepiness level and sleep quality level, patients with UC experienced higher levels of DA than those with CD. When we compared patients with HCs, we found that DA was higher in HCs than in the CD or UC groups. The interactive effect of study group and gender on DA was not significant after controlling for depression and anxiety levels, and sociodemographic data, as well as accounting for other sleep-related variables. DA has been investigated in several different clinical groups. In a previous study, patients with hypertension had higher DA levels than HCs [34]. Higher DA was found in patients with preeclampsia than in pregnant patients without preeclampsia [35]. In another study, no difference was found between renal transplantation receivers and healthy participants [36]. In hemodialysis patients, DA was found higher in those undergoing hemodialysis than healthy participants [37]. Nightmares also cause daytime sleepiness, and increased DA is also consistent with increased daytime sleepiness in HCs [38]. In previous studies, mean VDAS scores changed from 2.63 to 16.55 in HCs; compared to the mean VDAS score of our HC group at 10.23 [34, 36, 37]. Therefore, DA level in our HC group was consistent with the current literature and reliable.

In terms of sleepiness, we found no difference between patients with CD and those with UC, but sleepiness was higher in HCs than in patients with IBD. Similarly, a previous study reported no difference in sleepiness between patients with CD and those with UC; however, it had no control group so it is difficult to compare with our findings [39]. Several disorders such as obstructive sleep apnea, gastroesophageal reflux, or narcolepsy can cause daytime sleepiness, and our HCs may have had other causes of sleepiness than our patient groups. Another reason for higher sleepiness in HCs than patient groups may be that our HCs were informal caregivers of patients in outpatient clinics. Informal caregiving literature suggested higher levels of burden and disturbances in sleep patterns due to caring for ill significant others [40–42]. We recommend further studies to control for other sources of sleepiness in HCs when compared to patients with IBD.

In sum, our results suggest that women with CD may be at risk of having poorer sleep quality than men, regardless of health/IBD status. Moreover, patients with UC may be at a higher risk of experiencing DA than those with CD. In contrast, both patient groups seem to experience less sleep anxiety and less sleepiness than the HC group. This finding could be attributed to the differences in perceived social support. Social support is important in coping with disease and may also have some negative effects on patients [43]. In our study, patients with IBD reported lower anxiety and DA than HCs. Social support that they received during their disease course may decrease anxiety and causes lower DA in these patients. Our results also may reflect the burden of caregiving in our study population because the HC group consisted of healthy relatives of patients who are culturally supposed to be responsible from the daycare or night care of the patients.

A number of factors should be considered when interpreting the results of our study. Only outpatients who

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were in remission were included in this study. Previous studies have shown that anxiety and depressive symptoms are often found during relapses of IBD symptoms [44, 45]. This may explain why the rates of anxiety and depression, as well as DA, were lower in these patient groups. In addition, these patients were on medication. There is evidence that immunosuppressive medications (such as infliximab, adalimumab, certolizumab, methotrexate, and azathioprine) used to treat core IBD symptoms may be effective in treating depression in patients with IBD [46–48]. Because a complex relationship exists between psychiatric disorders and inflammation, the usage of anti-inflammatory agents may also affect the results.

Evaluating psychological factors with subjective questionnaires is one of the limitations of this study. Although validation and reliability studies exist for all the questionnaires used, the findings would be enriched by the inclusion of some biological indicators or examination by a psychiatrist. Another limitation was the lack of further evaluation of sleep quality and sleepiness. Evaluating the etiologies for these sleep disorders would provide us with better outcomes than the current results.

In conclusion, IBD is an intestinal disease that may be accompanied by sleeping disorders. In this study for the first time, we revealed that DA may be one of the factors leading to sleep disturbance in IBD. Future studies investigating the effect of DA on sleep and clinical course in patients with active IBD should help to better understand the role of sleep in IBD and develop future treatment.

Statement of Ethics

The study was approved by the local Ethics Committee (approval date: November 4, 2016, approval number: 09.2016.564).

Disclosure Statement

The authors declared no financial conflicts of interest.

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Author Contributions

H.T.K., A.S.K., O.A., K.K., and N.I.: conception and design of the study. H.T.K., E.B., C.A., and M.M.K.: acquisition of the data. H.T.K., A.S.K., U.D., and N.I.: analysis and interpretation of data. H.T.K., A.S.K., U.D., Y.O.A., O.A., K.K., and N.I.: critical revisions for important intellectual content. H.T.K., A.S.K., U.D., Y.O.A., O.A., K.K., and N.I.: final approval of the version to be submitted.

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