

Evaluation of latent links between irritable bowel syndrome and sleep quality

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Abstract

AIM: To examine the links between quality of sleep and the severity of intestinal symptoms in irritable bowel syndrome (IBS).

METHODS: One hundred and forty-two outpatients (110

female, 32 male) who met the Rome III criteria for IBS with no psychiatric comorbidity were consecutively enrolled in this study. Data on age, body mass index (BMI), and a set of life-habit variables were recorded, and IBS symptoms and sleep quality were evaluated using the questionnaires IBS Symptom Severity Score (IBS-SSS) and Pittsburgh Sleep Quality Index (PSQI). The association between severity of IBS and sleep disturbances was evaluated by comparing the global IBS-SSS and PSQI score (Pearson's correlation and Fisher's exact test) and then analyzing the individual items of the IBS-SSS and PSQI questionnaires by a unitary bowel-sleep model based on item response theory (IRT).

RESULTS: IBS-SSS ranged from mild to severe (120-470). The global PSQI score ranged from 1 to 17 (median 5), and 60 patients were found to be poor sleepers (PSQI > 5). The correlation between the global IBS-SSS and PSQI score indicated a weak association ($r = 0.2$ and 95% CI: -0.03 to 0.35, $P < 0.05$), which becomes stronger using our unitary model. Indeed, the IBS and sleep disturbances severities, estimated as latent variables, resulted significantly high intra-subject correlation (posterior mean of $r = 0.45$ and 95% CI: 0.17 to 0.70, $P < 0.05$). Moreover, the correlations between patient features (age, sex, BMI, daily coffee and alcohol intake) and IBS and sleep disturbances were also analyzed through our unitary model. Age was a significant regressor, with patients ≤ 50 years old showing more severe bowel disturbances (posterior mean = -0.38, $P < 0.05$) and less severe sleep disturbances (posterior mean = 0.49, $P < 0.05$) than older patients. Higher daily coffee intake was correlated with a lower severity of bowel disturbances (posterior mean = -0.31, $P < 0.05$). Sex (female) and daily alcohol intake (modest) were correlated with less severe sleep disturbances.

CONCLUSION: The unitary bowel-sleep model based on IRT revealed a strong positive correlation between the severity of IBS symptoms and sleep disturbances.

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Key words: Irritable bowel syndrome; Sleep disorders; Item response theory model; Bayesian model**Peer reviewer:** Guang-Yin Xu, MD, PhD, Assistant Professor, Division of Gastroenterology, Department of Internal Medicine, University of Texas Medical Branch, Galveston, TX 77555-0655, United States

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INTRODUCTION

Irritable bowel syndrome (IBS) is quite prevalent in the general population (5%-20%) and is in fact the functional gastrointestinal disorder most frequently encountered in primary and secondary care^[1,2]. IBS is characterized by abdominal discomfort, pain and changes in bowel habits (constipation and/or diarrhea)^[3]. Visceral hypersensitivity, slowed gastrointestinal transit, and alterations in secretion activity are also often reported^[4]. The direct and indirect costs of the syndrome are significant. IBS can have a serious impact on quality of life, and because it is often associated with other disorders, the patient may have to undergo expensive tests and treatments^[5-7].

Sleep disturbances connected with gastrointestinal functional disorders, in particular IBS, have been reported^[8-10], but no consistent abnormality in sleep patterns has been identified, apart from a significant increase in REM sleep^[11,12]. Many studies have associated sleep alterations with severity of IBS symptoms^[12], but it is not yet known whether there is a direct pathophysiological relationship^[13,14]. To date, a fundamental question remains - is sleep disturbance a cause or a consequence of IBS^[15]?

Growing awareness of the importance of the "brain-gut axis" has led some gastroenterologists to investigate sleep as an independent factor in the pathogenesis and clinical expression of IBS^[11,16].

The aim of the present study was to evaluate the association between the severity of sleep disturbances and intestinal symptoms, measured using two widely accepted questionnaires: the IBS Symptom Severity Score (IBS-SSS)^[17] and the Pittsburgh Sleep Quality Index (PSQI)^[18]. In addition, individual patient features were also analyzed to investigate their possible interaction with the severity of bowel and sleep disturbances and to exclude their potential confounding role.

MATERIALS AND METHODS

Study patients

Between October 2007 and September 2008, 142 patients

Table 1 Clinical subtypes, physical and life-habit variables of irritable bowel syndrome patients

	Item categories	Patients (%)
IBS subtype	M-IBS	29.6
	D-IBS	33.8
	C-IBS	36.6
Age (yr)	≤ 50	78.9
	> 50	21.1
Sex	Male	22.5
	Female	77.5
BMI (kg/m ²)	≤ 25	76.1
	> 25	23.9
Smoking	No	74.6
	Yes	25.4
Alcohol consumption	Non-/occasional drinkers	82.4
	Light drinkers (< 30 g ethanol/d)	17.6
Coffee consumption	< 2 cups/d	55.6
	> 2 cups/d	44.4
Physical activity	No	66.2
	Yes	33.8
Water consumption	< 1.5 L/d	61.3
	> 1.5 L/d	38.7

IBS: Irritable bowel syndrome; BMI: Body mass index.

who met the Rome III criteria for IBS^[3] with no confounding psychiatric comorbidity (diagnosed according to DSM IV axis I criteria) were consecutively enrolled from outpatients attending the Gastrointestinal Unit of the University of Pisa. All patients gave their informed written consent as required by the University Ethics Committee for Clinical Studies. The cohort was comprised of 110 female and 32 male patients (median age: 38 years; range: 18-79 years), of whom, 52 had constipation as the predominant symptom (C-IBS), 48 had diarrhea as the predominant symptom (D-IBS), and 42 had mixed symptoms (M-IBS).

We also evaluated physical and life-habit variables in each patient (Table 1): (1) sex and age; (2) body mass index (BMI)^[19]; (3) smoking; (4) alcohol intake^[20]; (5) coffee intake; (6) physical activity; and (7) water intake.

IBS and sleep questionnaires

IBS symptoms were evaluated using the IBS-SSS questionnaire^[17], which measured five separate items (Table 2): (1) presence and severity of abdominal pain or discomfort; (2) frequency of abdominal pain or discomfort; (3) presence and severity of abdominal distension; (4) degree of satisfaction with defecatory function; and (5) degree of interference of IBS symptoms with daily lifestyle. For each of the five items, the questions generated a score ranging from 0 to 100 that, for the purposes of analysis, was divided into three consecutive intervals: low, medium, and high (Table 2). The scores for the five items were summed to arrive at a global IBS-SSS (range: 0-500) and the IBS severity was then classified as mild (75-175), moderate (175-300) or severe (≥ 300).

Sleep quality was evaluated using the PSQI^[18], a self-administered questionnaire based on seven items: subjective sleep quality, sleep latency, sleep duration, habitual

Table 2 Distribution of responses to the items in the irritable bowel syndrome Symptom Severity Score across categories (low, medium and high)

IBS-SSS items	Category (score interval)	Patients (%)
Pain severity	Low: ≤ 40	31.0
	Medium: 40-70	43.7
	High: > 70	25.4
Pain frequency	Low: ≤ 20	19.7
	Medium: 20-70	33.8
	High: > 70	46.5
Distension	Low: ≤ 40	30.3
	Medium: 40-70	28.2
	High: > 70	41.5
Dissatisfaction with defecatory function	Low: ≤ 40	12.7
	Medium: 40-70	26.8
	High: > 70	60.6
Interference with daily life style	Low: ≤ 40	28.9
	Medium: 40-70	32.4
	High: > 70	38.7

IBS-SSS: Irritable bowel syndrome Symptom Severity Score.

sleep efficiency, sleep disturbances, use of sleep inducers, and daytime dysfunction. Each item was scored from 0 to 3, and the PSQI global index was calculated by summing these scores (range: 0-21); a global score > 5 identified poor sleepers.

In both questionnaires, lower values indicated lower severity, and higher values a more severe condition.

Statistical analysis

The association between the severity of IBS symptoms and sleep disturbances was first verified by directly comparing the global IBS-SSS and PSQI score, and then by evaluating the links between individual items in the two questionnaires.

For the first approach, we used both the Pearson correlation coefficient and the generalized Fisher exact test^[21]. The Pearson correlation measured the linear dependence between global scores, whereas the Fisher exact test verified the association between IBS-SSS and PSQI through a contingency table.

We adopted a unitary bowel-sleep model based on item response theory (IRT) that enabled us to investigate directly the dependences between IBS-SSS and PSQI single items. Furthermore, we also evaluated the weight of patient features and life habits in affecting the severity of IBS and sleep disturbances.

By focusing on individual items as the unit of analysis rather than the global score, the IRT model could circumvent the problem of different patterns of responses generating identical global scores. To this end, the values of both IBS-SSS single items and patient features were transformed in categories as indicated in the Tables 1 and 2. At variance, the PSQI items were not transformed since each item could have only four values (0-3), thus PSQI single item categories corresponded to the item values.

The output of our IRT model was the estimate of two latent variables: one related to the severity of IBS,

and the other to sleep disturbances. In order to evaluate the possible intra-subject associations between IBS and sleep disturbances, the latent variables for the two were jointly modeled using a bivariate normal distribution. The strength of this association was quantified by the covariance parameter. Specifically, we adopted the partial credit model^[22], which could be used for the polytomous ordered categories for each item. The partial credit model postulated that the probability of a given response with respect to the next response was a function (logistic curve) of the severity of the subject's symptoms and of structural parameters. The severity of symptoms, considered as a latent variable, was assumed to have a normal distribution^[23]. Finally, we used a regression model to remove the effects of the patient features from the latent severities, and to identify the features with a significant effect on each latent severity variable.

In the partial credit model analysis, a sum-to-zero constraint was imposed on the structural parameters^[24]. The model was estimated within a Bayesian framework by means of a Markov-chain Monte Carlo algorithm with Gibbs sampling (using WinBUGS 1.4)^[25]. This estimation required that one specified the prior distributions of all parameters, but in the present study, no such *a priori* information was available; thus non-informative priors (i.e. parameter-flat *a priori* distributions) were used.

The Bayesian method enabled us to estimate the distribution of each parameter (posterior distribution), from which we could derive the central tendency (posterior mean) along with the Bayesian confidence (or Credibility) interval (CI).

In summary, the unitary bowel-sleep model yielded estimates for each patient of the latent severity of their IBS and sleep disturbances, with their covariance parameters.

Finally, the mean latent severity of IBS and sleep disturbances were correlated with patient features (including IBS subtypes). One category was maintained as the reference and we verified whether the regression coefficient (posterior mean), describing the change from the reference to every other category, was significantly different from zero.

RESULTS

Analysis of the global scores

Patients had IBS-SSS ranging from 120 to 470 (median 280): 10 subjects were classified as mild, 69 as moderate, and 63 as severe. In Table 2, the distribution of responses to the items in the IBS-SSS across categories (low, medium and high) is shown.

The sleep quality in our patients ranged from 1 to 17, with a median PSQI score of 5. Sixty patients were poor sleepers (global PSQI > 5). The distribution of the scores for the items in the PSQI is shown in Table 3.

The correlation between the severity of IBS and sleep disturbances was evaluated by comparing the global IBS-SSS and PSQI scores. Pearson's *r* was found to be 0.2

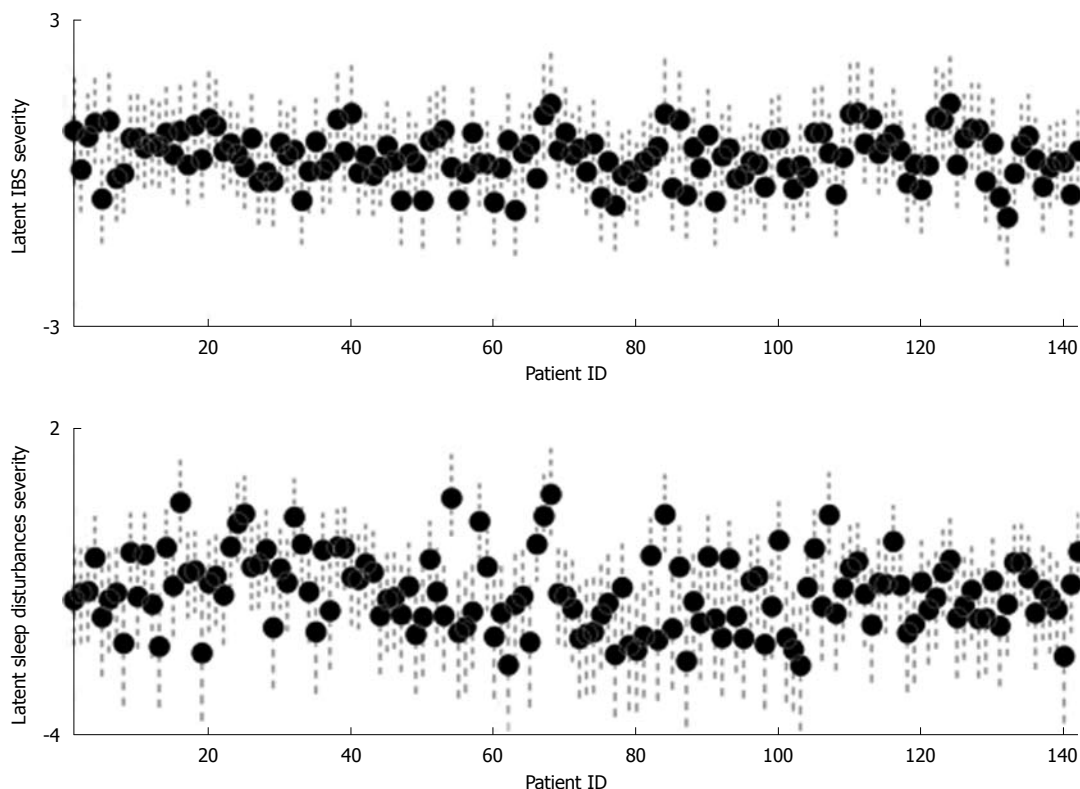


Figure 1 Irritable bowel syndrome latent severity in each patient, with 95% CI (top) and sleep disturbances latent severity in each patient, with 95% CI (bottom). Error bars indicate CI. ID indicates the label of each patient. IBS: Irritable bowel syndrome.

PSQI items	Item scores	Patients (%)
Subjective sleep quality	0	14.1
	1	62.7
	2	20.4
	3	2.8
Sleep latency	0	52.8
	1	28.2
	2	14.1
	3	4.9
Sleep duration	0	43.7
	1	35.9
	2	14.8
	3	5.6
Habitual sleep efficiency	0	54.9
	1	33.8
	2	7.7
	3	3.5
Sleep disturbances	0	8.5
	1	81.0
	2	9.9
	3	0.7
Use of sleeping medication	0	81.0
	1	3.5
	2	2.1
	3	13.4
Daytime dysfunction	0	31.0
	1	50.7
	2	13.4
	3	4.9

PSQI: Pittsburgh Sleep Quality Index.

	Global PSQI score	
	Good	Poor
Global IBS-SSS		
Mild	7	3
Moderate	44	25
Severe	31	32

IBS-SSS: Irritable bowel syndrome Symptom Severity Score; PSQI: Pittsburgh Sleep Quality Index.

(95% CI: 0.03 to 0.35), indicating a weak significant linear relationship between the two scores. Analysis of a contingency table for IBS-SSS *vs* PSQI categories using Fisher's exact test failed to detect any association between the two indices ($P = 0.18$) (Table 4).

Analysis of the latent severities

To complete the study of the questionnaires, the analysis was extended by modeling the responses to each single item with the partial credit models, and the regression analysis to determine the effect of the individual features on the estimated severity of IBS and sleep disturbances.

In Figure 1, the posterior means of the severity of IBS and sleep disturbances (expressed as latent variables) for the 142 patients are plotted (with their 95% CIs). The

Table 5 For each patient, feature regression coefficients (posterior means) and 95% CI for the latent severities of both irritable bowel syndrome and sleep disturbances are shown

Patient features	Categories	IBS latent severity, Coef (95% CI)	Sleep disturbances latent severity, Coef (95% CI)
IBS subtype	Mixed	0	0
	Diarrhoea	-0.10 (-0.45 to 0.24)	0.02 (-0.42 to 0.46)
	Constipation	0.32 (-0.05 to 0.69)	0.16 (-0.30 to 0.65)
Age (yr)	≤ 50	0	0
	> 50	-0.38 (-0.75 to -0.02) ¹	0.49 (0.02 to 0.96) ¹
Sex	Male	0	0
	Female	0.10 (-0.24 to 0.46)	-0.53 (-0.95 to -0.07) ¹
BMI (kg/m ²)	≤ 25	0	0
	> 25	0.04 (-0.32 to 0.38)	0.09 (-0.33 to 0.52)
Smoking	No	0	0
	Yes	0.07 (-0.27 to 0.41)	-0.04 (0.45 to 0.38)
Alcohol consumption	Non-/occasional drinkers	0	0
	light drinkers	-0.22 (-0.60 to 0.16)	-0.60 (-1.08 to -0.12) ¹
Coffee consumption	< 2 cups/d	0	0
	> 2 cups/d	-0.31 (-0.60 to -0.01) ¹	-0.08 (-0.44 to 0.26)
Physical activity	No	0	0
	Yes	-0.18 (-0.48 to 0.11)	-0.29 (-0.68 to 0.08)
Water consumption	< 1.5 L/d	0	0
	≥ 1.5 L/d	0.27 (-0.03 to 0.56)	0.07 (-0.29 to 0.42)

¹Significant differences between covariables. IBS: Irritable bowel syndrome.

latent severity of sleep disturbances was a better discriminant between subjects than IBS, since it showed a more marked between-subject variability: all of the patients had *a priori* IBS symptoms, whereas the quality of their sleep was measured for the first time in this study.

Our unitary bowel-sleep model demonstrated a significant association between the severity of bowel symptoms and sleep disturbances. In contrast to the results of the global score comparison, a significant intra-subject correlation was found (posterior mean $r = 0.45$ and 95% CI: 0.17 to 0.70).

Figure 2 shows two scatter plots, on the left the IBS-SSS and PSQI global scores, whereas on the right, the two latent severities. The usage of the unitary bowel-sleep model provided a relationship between latent sleep disturbances severity and latent IBS severity. At variance, the usage of global scores did not provide any information about sleep and bowel dysfunction interactions. In the right panel of Figure 2, each black dot corresponds to a single patient and the dashed grey cross indicates the respective CI. Despite the variability between patients, the correlation between the two latent severities was evident, while the scatter plot on the left panel did not confirm any association between the global scores.

Furthermore, the unitary bowel-sleep model allowed us to identify a significant regression between IBS and sleep disturbances latent severities and patient features (Table 5).

The significance of a feature effect corresponded to a significant regression coefficient, and the sign of this coefficient indicated the direction of the relationship: a positive sign signified that the change of category (from the reference one to the other) came with a severity increase and *vice versa*; the 95% CI indicated the significance of the coefficient.

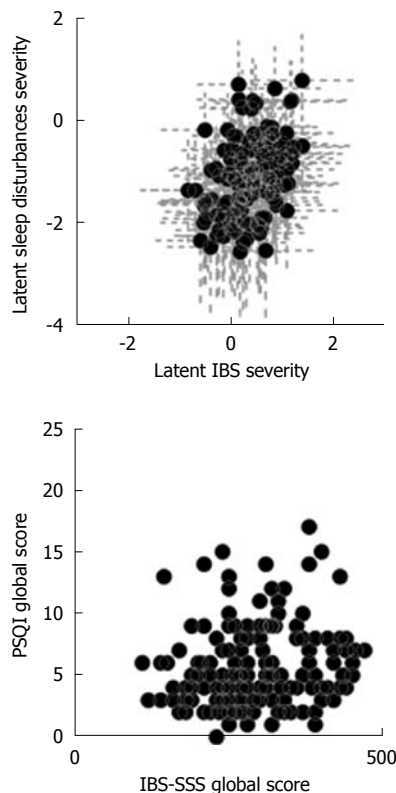


Figure 2 Scatter plot of the global Pittsburgh Sleep Quality Index score vs the global irritable bowel syndrome-Symptom Severity Score (left panel), and of sleep disturbances and irritable bowel syndrome latent severities (dots) (right panel). The grey lines indicate the 95% CI.

Among the individual features, age was a significant regressor for both latent severities; young patients (≤ 50 years old) showed more severe bowel disturbances (posterior mean = -0.38) and less severe sleep distur-

bances (posterior mean = 0.49) than older patients. Daily coffee intake was significantly correlated with severity of bowel disturbances (posterior mean = -0.31); subjects who consumed ≥ 2 cups per day showed less severe bowel disturbances. Sex and daily alcohol intake were found to be significantly correlated with severity of sleep disturbances; female patients exhibited less severe sleep disturbances than male patients, while non-drinkers showed more severe sleep disturbances than those with a moderate alcohol intake. No other life-habit variables were found to be significantly correlated with latent severity of IBS or sleep disturbances.

DISCUSSION

The aim of this study was to evaluate the mutual influences between sleep disturbances and IBS in a large sample of IBS patients. The study provides a detailed statistical analysis of the possible association between bowel disorders, sleep disturbances and life habits.

Our sample may be considered as representative of the IBS population in Italy (this was confirmed by the distribution of IBS subtypes, age and BMI in the cohort). Therefore, our results can be compared and discussed in the light of the results of other studies on IBS patients.

Despite the fact that 42% of the participants had a global PSQI score > 5 , only a weak and ambiguous association between IBS-SSS categories and PSQI categories was evident by using standard statistical analysis. Indeed, the correlation coefficient between the global scores was weakly significant and the Fischer exact test did not yield any association.

Conversely a strong link was highlighted by applying the IRT model^[26,27] and linear regression.

IRT provides a framework to detect the effect of a series of variables (such as the responses to items on psychological tests) on latent traits of interest (IBS and sleep disturbances). In standard data analyses, the patient's raw score is calculated by summing the scores for the different items, without taking into account differences in the responses to specific items by different patients. It may arise that two patients have the same raw global score but different patterns of symptoms, or different raw global scores but similar symptom patterns. The inability to discriminate between the two possibilities can be resolved by using IRT model, which focuses on individual items rather than the global score. In addition, IRT allows one to introduce covariates (in our case age, BMI, and life habits) and analyze their effect on the parameters of interest.

The IRT model identified a latent link between sleep disturbances and IBS symptoms. These results showed that IBS patients suffered from a considerable degree of sleep impairment, and are in line with those of other studies^[8,28,29]. In particular, a recent survey found that sleep disturbances were an independent predictor of IBS in nurses^[8].

Through IRT analysis, we also determined that older

age, male sex, and no alcohol intake were significant predictors of more severe sleep disturbances.

Our study found that female IBS patients complained with fewer sleep disturbances than males. This would appear to be inconsistent with studies in the general population, which show that females are more likely to suffer from sleep disorders^[30], more susceptible to the effects of stress on sleep^[31], and after menopause, run a higher risk of developing insomnia^[30]. The present findings could be explained by the demographics of our sample, which were characterized by a relatively low mean age and hence a higher percentage of fertile women; indeed, IBS patients tend to be relatively young (< 50 years old)^[3].

Evaluation of the predictive parameters for the latent severity of sleep disorders showed that age was positively correlated with sleep disturbances. These data come as no surprise, because aging is widely considered to be a triggering factor for insomnia^[32-34].

Finally, this study showed that light alcohol intake was correlated with a lower latent severity of sleep disturbances. It has long been known that a little amount of alcohol consumed by healthy individuals before going to sleep shortens sleep latency, reduces REM sleep, and increases non-REM sleep^[35-39]. Alcohol is frequently used as a form of self-medication by patients suffering from sleep disorders, especially insomnia^[40].

More unexpectedly, we found that younger age and higher coffee intake were associated with less severe IBS symptoms. The first-line treatment for IBS usually consists of a change in lifestyle and diet, and drinking less coffee is often recommended, even though there are no studies demonstrating a link between the consumption of coffee and the severity of IBS symptoms. Sloots *et al*^[41] have reported that the intake of 280 mL of coffee caused no change in rectal compliance or visceral sensibility. However, in our study, coffee drinkers actually consumed no more than two cups per day.

In conclusion, using IRT analysis we found that: (1) there was a positive association between the severity of IBS symptoms and sleep disturbances, and (2) some patient features were significant predictors of severity of IBS and sleep disturbances. These results are consistent with those of other studies^[10,14]. The pathophysiological mechanism underlying this association is only partially understood, however. One possibility is that sleep disorders can induce visceral hyperalgesia, which increases the patient perception of gastrointestinal symptoms^[8,15]. Several other factors could play a role, including endophenotypic traits such as those associated with stress susceptibility^[42].

Further research is needed to clarify whether the association of IBS and sleep disturbances represents comorbidity or the expression of a single disturbance in the brain-gut axis.

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COMMENTS

Background

Sleep disturbances connected with gastrointestinal functional disorders, in particular irritable bowel syndrome (IBS), have been reported and some studies have associated sleep alterations with the severity of IBS symptoms. It is not yet known whether it is a simple comorbidity or if there is a direct pathophysiological relationship. To date, a fundamental question has arisen: is sleep disturbance a cause or a consequence of IBS?

Research frontiers

Sleep disturbances represent a negative factor affecting the outcome of several medical and psychiatric conditions, therefore, growing awareness has led some gastroenterologists to investigate sleep as an independent factor also in the pathogenesis and clinical expression of IBS.

Innovations and breakthroughs

Item response theory (IRT) for the first time has been used to identify latent links between digestive symptoms and sleep quality. Furthermore, this unitary bowel-sleep model enabled us to evaluate better the weight of patient features and life habits in the severity of IBS symptoms and sleep disturbances.

Applications

The results of this study suggest: (1) the use of IRT models for uncovering latent links in clinical comorbidity; (2) the importance of studying sleep quality in functional digestive disorders; and (3) further surveys on the clinical mutual interaction between sleep disturbances and functional digestive disorders (i.e. if the treatment of sleep disturbances improves digestive symptoms and/or vice versa)

Terminology

IRT is a paradigm for the analysis of tests and questionnaires. IRT models are often referred to as "latent trait models". The term latent is used to emphasize discrete item responses not directly observed but inferred from the manifest responses. IRT brings greater flexibility and provides more sophisticated information and is generally considered an improvement of classical test theory. The Bayesian method enables one to estimate the distribution of each parameter from which one could derive the central tendency.

Peer review

The authors have looked at sleep quality in patients with IBS to evaluate the relationship between digestive symptoms and sleep quality by using IRT analysis. The results are analyzed in detail and the statistical tool of IRT is used to obtain significant associations. The data are solid, the paper is interesting, has clinical significance and is well written.

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