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SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Somatic syndromes, insomnia, anxiety, and stress among sleep disordered breathing patients

Tshering Amdo[1,2] · **Nadia Hasaneen**[1,2] · **Morris S. Gold**[3] · **Avram R. Gold**[1,2]

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Abstract
Objectives We tested the hypothesis that the prevalence of somatic syndromes, anxiety, and insomnia among sleep disordered breathing (SDB) patients is correlated with their levels of somatic arousal, the symptoms of increased sympathetic nervous system tone under conditions of stress.
Methods We administered the Body Sensation Questionnaire (BSQ; a 17-item questionnaire with increasing levels of somatic arousal scored 17–85) to 152 consecutive upper airway resistance syndrome (UARS) patients and 150 consecutive obstructive sleep apnea/hypopnea (OSA/H) patients. From medical records, we characterized each patient in terms of the presence of syndromes and symptoms into three categories: somatic syndromes (six syndromes), anxiety (anxiety disorders, nightmares, use of benzodiazepines), and insomnia (sleep onset, sleep maintenance, and use of hypnotics). For the pooled sample of SDB patients, we modeled the correlation of the BSQ score with the presence of each syndrome/symptom parameter within each of the three categories, with adjustment for male vs. female.
Results Mean BSQ scores in females were significantly higher than those in males (32.5 ± 11.1 vs. 26.9 ± 8.2; mean ± SD). Increasing BSQ scores significantly correlated with increasing prevalence rates of somatic syndromes ($p < 0.0001$), of anxiety ($p < 0.0001$), and of insomnia ($p \leq 0.0001$). In general, females had higher prevalence rates of somatic syndromes and symptoms of anxiety than males at any BSQ score while rates of insomnia were similar.
Conclusions In patients with SDB, there is a strong association between the level of somatic arousal and the presence of stress-related disorders like somatic syndromes, anxiety, and insomnia.

Keywords Upper airway resistance syndrome · Sleep disordered breathing · Chronic stress · Somatic arousal · Sympathetic nervous system · Central sensitization syndromes · Body Sensation Questionnaire

Introduction

Somatic syndromes, chronic insomnia, and anxiety are often observed in the same individuals. Somatic syndromes, also termed *functional* somatic syndromes [1], are medically unexplained symptoms or somatoform disorders [2], exemplified by migraine headache/tension headache syndrome, irritable bowel syndrome (IBS), temporomandibular joint (TMJ) syndrome, and fibromyalgia (there are many others) [1, 2]. Most of these syndromes affect primarily women and include a form of body pain in association with fatigue, chronic insomnia, cognitive dysfunction, anxiety, or depression, symptoms which are commonly associated with chronic stress [3, 4]. Thus, somatic syndromes, chronic insomnia, and anxiety are hypothesized to be the consequences of chronic stress [5–7].

Somatic syndromes, chronic insomnia, and anxiety are also hypothesized to be the consequences of obstructive sleep apnea/hypopnea (OSA/H) and upper airway resistance syndrome (UARS). Inspiratory airflow limitation (IFL) during

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✉ Avram R. Gold
avram.gold@va.gov

[1] Division of Pulmonary/Critical Care/Sleep Medicine, Stony Brook University School of Medicine, Stony Brook, NY 11794, USA

[2] DVA Medical Center, Northport, NY 11768, USA

[3] GlaxoSmithKline Consumer Health, Parsippany, NJ 07054, USA

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sleep is common among patients with IBS [8], irritable bladder syndrome [9], TMJ syndrome [10], fibromyalgia [11], and Gulf War illness [12]. Furthermore, pharyngeal splinting during sleep with nasal continuous positive airway pressure (CPAP) has been shown to alleviate the symptoms of such patients [11, 13]. Chronic insomnia and anxiety are also commonly associated with sleep disordered breathing (SDB) [14, 15].

A recent study by Gold and associates [16] supports a new paradigm that integrates the preceding observations regarding chronic stress and SDB as causes and somatic syndromes, chronic insomnia, and anxiety as effects. Since early 2008, all patients treated at the Stony Brook University Sleep Disorders Center have been assessed for levels of somatic arousal, which are the physical manifestations of the sympathetic nervous system (SNS) component of the stress response, using a validated 17-item questionnaire. They have also completed standard self-report assessments of both sleepiness and fatigue. A clinical series of 302 patients with either OSA/H or UARS was extracted in which initial assessments of somatic arousal, sleepiness, and fatigue were available from all patients and from 94 of the patients (31 %) after treatment with nasal CPAP [16]. Both the OSA/H and UARS patients demonstrated comparably elevated initial levels of self-reported somatic arousal (elevated levels of stress), and in both groups, the initial level of somatic arousal was significantly correlated with levels of both sleepiness and fatigue. With nasal CPAP treatment, somatic arousal, sleepiness, and fatigue decreased significantly and the decrease in somatic arousal was significantly correlated with the decrease in the level of fatigue. The authors concluded with the hypothesis that OSA/H and UARS share a pathophysiologic pathway of chronic stress related to the nightly presence of IFL during sleep that may be an important cause of their sleepiness and fatigue.

The presence of stress measured as somatic arousal among patients with SDB predicts that conditions associated with chronic stress, the somatic syndromes, chronic insomnia, and anxiety, will occur with elevated frequency in these patients. Moreover, among SDB patients, those with the highest levels of stress should experience the highest prevalence of somatic syndromes, chronic insomnia, and anxiety. To investigate the hypothesis that among SDB patients, increased levels of stress are associated with increased prevalence of somatic syndromes, chronic insomnia, and anxiety, we used the same clinical series of 302 OSA/H and UARS patients [16], their anthropometric data, and medical histories. With this data, we examined the correlates of increased somatic arousal in SDB patients and we characterized the relationship between level of somatic arousal and prevalence rates of somatic syndromes, chronic insomnia, and anxiety.

Methods

Participant selection

Our methods for participant selection have been detailed previously in our study of somatic arousal and sleepiness/fatigue among SDB patients [16] and will be summarized here. Consecutive series of patients with UARS and OSA/H diagnosed by one physician (ARG) and treated at the SBU Sleep Disorders Center between January 2008 and December 2012 were identified retrospectively. The protocol was approved by the SBU Institutional Review Board.

Inclusion criteria for UARS patients differed from those for OSA/H patients. For UARS, we included 152 consecutive patients over the 2008–2012 period who were newly diagnosed (not being treated with upper airway stabilization during sleep at their initial consultation) and whose charts included an initial Body Sensation Questionnaire (BSQ), a sleep-oriented history and physical examination, and a diagnostic polysomnogram. Patients diagnosed with UARS complained of sleepiness or fatigue without meeting diagnostic criteria for narcolepsy, had an apnea-hypopnea index (AHI) < 10/h, and demonstrated IFL during NREM sleep determined by pressure transducer airflow (there was no RERA frequency threshold required for the diagnosis). Patients with symptoms of RLS were not excluded because RLS is considered one of the somatic syndromes [17] and is commonly observed among SDB patients [18, 19].

To compare with these UARS patients, we selected three groups of 50 consecutive patients, based upon AHI, newly diagnosed with OSA/H and classified as $10 \leq \text{AHI} < 30$, $30 \leq \text{AHI} < 60$, and $60 < \text{AHI}$. Each group was obtained by starting with patients seen in December 2012 and moving consecutively backward in time giving precedence to patients undergoing treatment with nasal CPAP and providing post-treatment questionnaire data and a compliance report for the longitudinal component of our previous study [16]. The charts of the selected OSA/H patients all included the initial assessment of somatic arousal, a sleep-oriented history and physical examination, and a diagnostic polysomnogram, required for this study.

Data selection

Anthropometric and polysomnographic data

Anthropometric data (age, sex, body mass index) and the AHI utilized to group patients into SDB categories were obtained from the diagnostic polysomnogram performed at the Stony Brook University Sleep Disorders Center (an AASM-accredited center following recommended staging and respiratory scoring criteria [20]).

Sleep and medical history data

Each Stony Brook University Sleep Disorders Center patient assessed the frequency of 24 sleep-related complaints on a 4-point scale: 0 = never/rarely, 1 = 1×/week, 2 = 2–4×/week, and 3 = almost always. From each patient's chart, the frequency of the following complaints was extracted:

(1) Experience restlessness or discomfort in the legs (restless legs syndrome; RLS)
(2) Have difficulty falling asleep (insomnia)
(3) Lie awake with intense thoughts (insomnia)
(4) Wake up during the night (insomnia)
(5) Experience nightmares (anxiety)

These complaints were dichotomized as 0/1 = absence and 2/3 = presence, so that the presence of each complaint meant it occurs more than once per week.

Presence of the following diagnoses/symptoms was extracted from the Sleep Disorders Center's medical history questionnaire and standardized Sleep Medicine note (both sources make specific reference to the diagnoses/symptoms): chronic fatigue syndrome (CFS), fibromyalgia, IBS, TMJ syndrome, headaches (excluding morning headaches), and anxiety (an anxiety disorder or anxiety as a symptom in review of systems). From the medication list, we recorded whether or not benzodiazepines or hypnotics were used. The physician's dictated consultation was also reviewed (when available).

Self-report somatic arousal data

Somatic arousal, the SNS component of the stress response, was quantified with the BSQ (the Mood and Anxiety Symptom Questionnaire Anxious Arousal Subscale; ESM 1). The BSQ is a 17-item questionnaire in which the respondent rates how much a symptom or sign of increased SNS tone was experienced over the preceding week on an increasing scale from 1 (never) to 5 (extremely). Increasing BSQ total scores reflect increasing somatic arousal with a range of 17 to 85.

Statistics

In the primary study of this sample of UARS and OSA/H patients, Gold and associates [16] examined the relationship between BSQ score and fatigue and sleepiness, the cardinal symptoms of SDB. The identified relationship was the same in both populations, despite their large differences in AHI and oxygen saturation during sleep. Consequently, for the present analysis, the two populations were pooled. (The supplement considers the impact of AHI on the prevalence of somatic syndromes, of anxiety, and of insomnia; ESM 2.)

The various syndromes/parameters whose prevalence we consider were assigned to three parameter groups, the somatic syndromes (headache and five syndromes), anxiety (three parameters), and insomnia (four parameters). As an initial characterization of the impact of increasing BSQ score, for each parameter group, a table shows crude prevalence rates as a function of trichotomized BSQ score (≤25, 26–35, >35) and of sex, a known risk factor for the somatic syndromes with females having a higher prevalence [21–24]. The prevalence rate of each parameter was then modeled with logistic regression as a function of BSQ score and sex. To address the correlation induced by modeling the prevalence rates of multiple parameters within each parameter group over the same population of patients, the logistic regressions were incorporated into a generalized linear mixed model with random intercept (assumed normally distributed over patients with mean 0 and variance τ (the variance component model)) and fixed effects for BSQ score and sex. More complicated covariance structures do not materially change the model results. The statistical significance of each term in the model was tested with an F-test. To illustrate the final selected statistical model for each parameter group, a figure shows the expected prevalence of each parameter as a function of increasing BSQ score, by sex.

The relationship between BSQ score and the number of somatic syndromes per subject was summarized as (a) the mean number of somatic syndromes per subject over all subjects in each of the three BSQ categories and (b) the mean BSQ score over all subjects with the same number of somatic syndromes. The number of somatic syndromes per subject was then modeled with Poisson regression as a linear function of BSQ score and sex.

All computations were done using PROC GLIMMIX in SAS Version 9.3 [25].

Results

Table 1 summarizes anthropometrics over the 152 consecutive UARS patients and the three groups of 50 consecutive OSA/H patients. Consistent with this group's previous studies [26, 27], the UARS patients were younger and leaner with a much higher percentage of females vs. the OSA/H patients.

In the primary study done with this data [16], Gold and associates found no relationship between BSQ score and SDB severity. The BSQ score of the UARS sample (30 ± 10; mean ± SD) was the same as for the most severe OSA/H sample (29 ± 9) despite markedly different group means for the apnea-hypopnea index (4.3 ± 3.1 vs. 80.2 ± 16.7) and time spent at or above an oxygen saturation of 90 % (95.9 ± 13.4 vs. 49.8 ± 34.2 %). However, BSQ scores for the 104 females (32.5 ± 11.1) were systematically higher than those for the 298 males (26.9 ± 8.2; $p < 0.0001$ by unpaired T test (Fig. 1)).

Table 1 Anthropometric data for the sleep disordered breathing patients

Parameters	UARS	10 ≤ AHI < 30	30 ≤ AHI < 60	AHI ≥ 60
Patient number	152	50	50	50
Anthropometric data				
Sex (% female)	50	26	16	16
Age (years)	43.5 ± 15.4	52.6 ± 11.7	54.3 ± 13.5	48.6 ± 12.0
Body mass index (kg/m^2)	28.3 ± 7.2	31.2 ± 6.5	33.7 ± 6.7	40.4 ± 8.8

UARS upper airway resistance syndrome, *AHI* apnea-hypopnea index

Somatic arousal and prevalence of the somatic syndromes

Six somatic syndromes were considered: headaches, RLS, TMJ, IBS, fibromyalgia, and CFS. In Table 2, crude prevalence rates of each somatic syndrome are shown for the pooled SDB population by sex, for the three subgroups of increasing BSQ score. Prevalence rates of somatic syndromes were generally 2× to 4× higher in females than in males, except for RLS which was similarly prevalent. Thus, half of females reported headaches; a quarter reported each of IBS, RLS, and TMJ; and roughly 15 % reported each of fibromyalgia and CFS. In contrast, headaches and RLS affected 20–25 % of males, IBS and TMJ affected 5–10 %, and fibromyalgia and CFS affected fewer than 5 %.

In females, as BSQ score increased, the prevalence of each somatic syndrome increased. Headache prevalence increased from 39 % in the lowest subgroup of BSQ score to 56 % in the highest subgroup of BSQ score, a relative increase of roughly 40 %. Correspondingly, the rate of CFS increased by about 60 % (from 14.3 to 23.3 %), the rate of IBS increased by about 75 %, the rates of RLS and TMJ roughly doubled, and the rate of fibromyalgia almost tripled.

In males, the pattern is more variable. There was no clear increase in prevalence rates for either headache or TMJ as BSQ score increased from the lowest to the highest subgroup. However, the prevalence rate of IBS more than doubled (from 13.5 to 37.0 %); for RLS and CFS, it almost tripled; and for fibromyalgia, it almost quadrupled (from 2.9 to 11.1 %).

The relationship between prevalence rates, sex, and BSQ score in the six somatic syndromes was modeled over the pooled SDB population with multivariate logistic regression. The best fitting model included separate *Y* intercepts for males and for females for each somatic syndrome (12 intercepts; syndrome*sex interaction) and a slope of the BSQ score that was common to both females and males for each somatic syndrome (six slopes; syndrome*BSQ score interaction). The separate *Y* intercepts for females and males for each somatic syndrome reflect the finding in Table 2 that for each syndrome (except for RLS), prevalence rates for females were generally two to four times higher than those for males.

Figure 2 illustrates the results of the regression model, in which prevalence rates of the various somatic syndromes increased with increasing BSQ score. The *p* values establish the statistical significance of the BSQ score as a predictor of

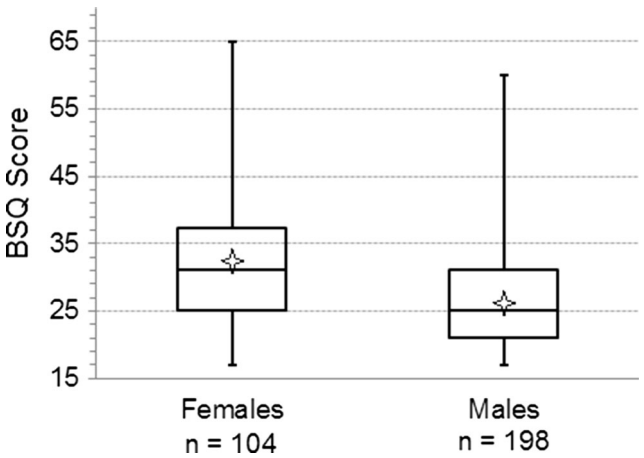

Fig. 1 Box-and-whisker plot illustrating the Body Sensation Questionnaire (BSQ) scores for the 104 female and 198 male consecutive patients with sleep disordered breathing included in this study. The *upper and lower sides of each box* indicate the BSQ scores at the upper quartile and lower quartile of each data set, while the *line running through each box* indicates the median BSQ score. The *lower whisker* extends from the lowest measured BSQ score (17, the minimum BSQ score in each data set) to the score at the lower quartile, and the *upper whisker* extends from the BSQ score at the upper quartile to the highest measured BSQ score in each data set. The *star in each box* indicates the mean BSQ score for each data set

Table 2 Prevalence rates for somatic syndromes in SDB patients based upon sex and BSQ score

	Females				Males			
	BSQ scores				BSQ scores			
	≤25	26–35	>35	All	≤25	26–35	>35	All
Patient numbers	28	46	30	104	104	67	27	198
CFS (%)	14.3	13.0	23.3	16.4	3.9	0	11.1	3.5
Fibromyalgia (%)	7.1	13.0	20.0	13.5	2.9	3.0	11.1	4.0
Headaches (%)	39.3	56.5	56.7	51.9	22.1	22.4	18.5	21.7
IBS (%)	21.4	26.1	36.7	27.9	7.7	11.9	18.5	10.6
RLS (%)	17.9	23.9	36.7	26.0	13.5	29.9	37.0	22.2
TMJ (%)	17.9	23.9	33.3	25.0	7.7	6.0	7.4	7.1

CFS chronic fatigue syndrome, *IBS* irritable bowel syndrome, *RLS* restless legs syndrome, *TMJ* temporomandibular joint syndrome

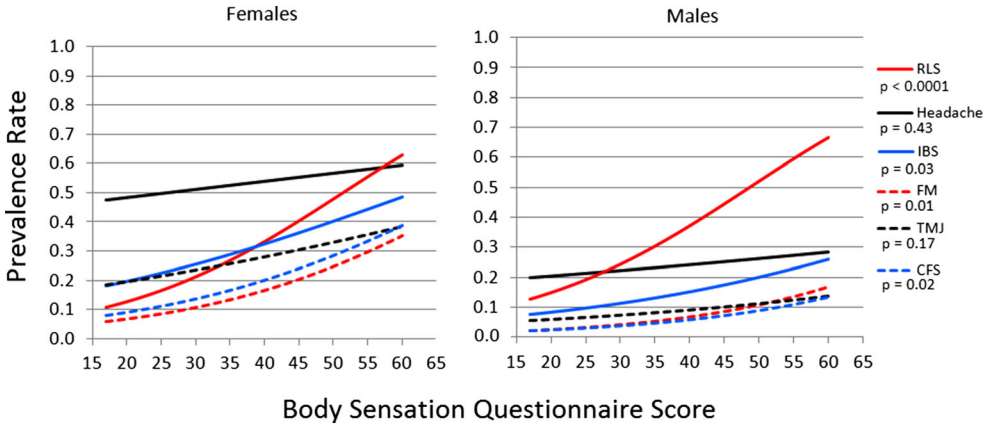

Fig. 2 The results of the regression model relating prevalence rates of the six somatic syndrome parameters to increasing BSQ score for females and males with sleep disordered breathing. The *p* values for each parameter reflect the statistical significance of the correlation between prevalence rate and BSQ score for the combined samples (females and males). *RLS* restless legs syndrome, *IBS* irritable bowel syndrome, *FM* fibromyalgia, *TMJ* temporomandibular joint syndrome, *CFS* chronic fatigue syndrome. The figure is further explained in the text

prevalence for each somatic syndrome. Overall, the BSQ score was a highly significant predictor of somatic syndromes ($p < 0.0001$), driven by statistically significant *p* values for RLS, IBS, fibromyalgia, and CFS. The *p* values of 0.43 and 0.17 for headache and TMJ reflect the finding in Table 2 of no correlation in males between BSQ score and prevalence rates.

Somatic arousal and number of somatic syndromes per patient

Table 3 illustrates the relationship between increasing numbers of somatic syndromes per patient and increasing BSQ score. The average female had more than twice as many FSS as the average male (1.6 vs. 0.7). Among females, the mean BSQ score progressively increased as the number of somatic syndromes increased. The relationship was more variable in males. In both females and males, as BSQ score increased, there was a steady increase in the mean number of somatic syndromes with a constant 2× ratio between sexes.

In a Poisson regression with separate *Y* intercepts for females and males, increasing BSQ score significantly predicted an increasing number of somatic syndromes per patient ($p < 0.0001$).

Table 3 The number of somatic syndromes per patient as a function of BSQ score

Sex	Syndromes (number)	Patients (number)	BSQ score Mean (SD)
Females	0	21	27.5 (7.9)
	1	32	29.9 (9.7)
	2	44	34.4 (10.5)
	3, 4, 5	24	38.3 (13.2)
Males	0	97	24.0 (6.4)
	1	72	30.3 (9.1)
	2	22	26.6 (6.9)
	3	7	32.0 (11.2)
Sex	BSQ score	Patients (number)	Syndromes (number) Mean (SD)
Females	≤25	28	1.18 (1.19)
	26–35	46	1.57 (1.20)
	>35	30	2.07 (1.17)
Males	≤25	104	0.58 (0.83)
	26–35	67	0.73 (0.71)
	>35	27	1.04 (0.85)

Somatic arousal and prevalence of anxiety

Three anxiety parameters were considered: presence of an anxiety disorder/symptom, nightmares, and taking benzodiazepines. In Table 4, crude prevalence rates of each anxiety parameter are shown by sex for the three subgroups of increasing BSQ score, over the pooled SDB population. Prevalence rates of the various anxiety parameters were generally higher for females than for males. Thus, half of females reported an anxiety disorder/symptom and nightmares vs. about a third of males. Use of benzodiazepines was generally less common but much more frequent in females.

In both sexes, with increasing BSQ score, the prevalence of each anxiety parameter increased, except for use of benzodiazepines among males. Indeed, in the highest BSQ score subgroup, the prevalence of anxiety parameters explodes. In females, 83 % reported an anxiety disorder/symptom, 73 % reported nightmares, and over a quarter took benzodiazepines. Correspondingly, over half of males reported anxiety disorder/symptoms and nightmares, though only 7 % reported use of benzodiazepines.

The relationship between prevalence rates, sex, and BSQ score in the three anxiety parameters was modeled over the pooled SDB population with multivariate logistic regression.

Table 4 Prevalence rates for anxiety outcomes in SDB patients based upon sex and BSQ score

	Females				Males			
	BSQ values				BSQ values			
	≤25	26–35	>35	All	≤25	26–35	>35	All
Patient numbers	28	46	30	104	104	67	27	198
Anxiety (%)	32.1	39.1	83.3	50.0	24.0	35.8	51.9	31.8
Nightmares (%)	32.1	43.5	73.3	49.0	22.1	43.3	51.9	33.3
Benzodiazepines (%)	14.3	10.9	26.7	16.4	5.8	1.5	7.4	4.6

Anxiety an anxiety disorder or the complaint of anxiety on review of systems

The best fitting model included separate *Y* intercepts for males and for females for each anxiety parameter (six intercepts; parameter*sex interaction) and a slope of the BSQ score that was common to both females and males for each anxiety parameter (three slopes; parameter*BSQ score interaction).

Figure 3 illustrates the results of the regression model in which prevalence rates of the various anxiety parameters increased with increasing BSQ score. The *p* values establish the statistical significance of the BSQ score as a predictor of prevalence for each anxiety parameter. Overall, the BSQ score was a highly significant predictor of anxiety ($p < 0.0001$), driven by statistically significant *p* values for the presence of anxiety disorder/symptom and nightmares. The *p* value of 0.18 for use of benzodiazepines reflects the finding in Table 4 of no correlation in males between increasing BSQ score and use of benzodiazepines.

Somatic arousal and prevalence of insomnia

Four insomnia parameters were considered: (a) trouble falling asleep, (b) lying awake with intense thoughts, (c) waking up during the night, and (d) taking hypnotics. We consider (a) and (b) as reflecting sleep-onset insomnia whereas (c) reflects sleep-maintenance insomnia. In Table 5, crude prevalence rates of each insomnia parameter are shown by sex for the pooled SDB population, for the three subgroups of increasing BSQ score. Prevalence rates of the various insomnia parameters were roughly comparable for males and females. Sleep-maintenance insomnia was reported by 75–80 % of the population and sleep-onset insomnia by 25–40 %. Use of hypnotics was generally low.

In both sexes, with increasing BSQ score, the prevalence of each insomnia parameter increased. The prevalence of sleep-maintenance insomnia, already at roughly 75 % in the lowest BSQ score subgroup, increased to 85–90 % in the highest subgroup. The prevalence of sleep-onset insomnia doubled from roughly 20–30 % in the lowest BSQ score subgroup to roughly 50 % in the highest BSQ score subgroup. Prevalence of use of hypnotics increased steadily with increasing BSQ score, but was not appreciable even at the highest BSQ scores.

The relationship between prevalence rates, sex, and BSQ score in the four insomnia parameters was modeled over the pooled SDB population with multivariate logistic regression. The model included separate *Y* intercepts for males and for females for each insomnia parameter (eight intercepts;

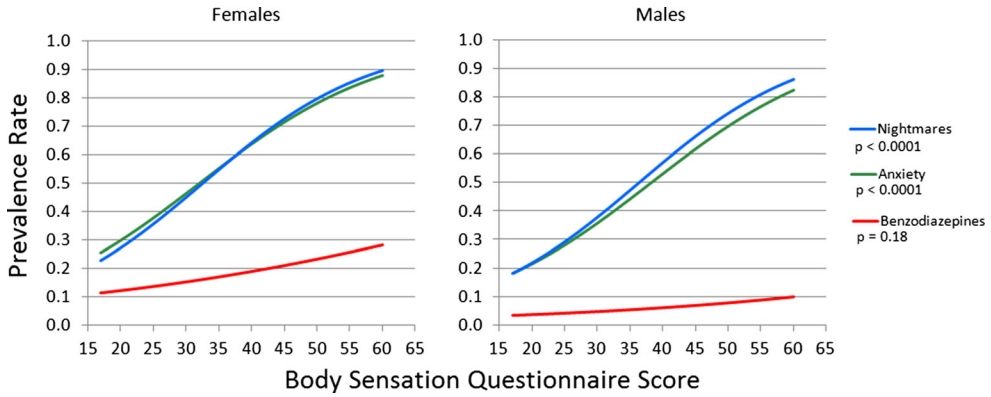

Fig. 3 The results of the regression model relating prevalence rates of the three anxiety parameters to increasing BSQ score for females and males with sleep disordered breathing. The *p* values for each parameter reflect the statistical significance of the correlation between prevalence rate and BSQ score for the combined samples (females and males). *Nightmares* experiences nightmares at least once weekly, *Anxiety* has a diagnosed anxiety disorder or the complaint of anxiety on review of systems, *Benzodiazepines* has a prescription for benzodiazepines. The figure is further explained in the text

Table 5 Prevalence rates for insomnia outcomes in SDB patients based upon sex and BSQ score

	Females				Males			
	BSQ values				BSQ values			
	≤25	26–35	>35	All	≤25	26–35	>35	All
Patient numbers	28	46	30	104	104	67	27	198
Cannot fall asleep (%)	39.3	37.0	53.3	42.3	22.1	34.3	55.6	30.8
Intense thoughts (%)	21.4	26.1	53.3	32.7	18.3	31.3	44.4	26.3
Awaken during the night (%)	78.6	73.9	90.0	79.8	70.2	77.6	85.2	74.8
Hypnotics (%)	10.7	15.2	23.3	16.4	6.7	11.9	14.8	9.6

parameter*sex interaction) and a slope of the BSQ score that was common to both males and females for each insomnia parameter (four slopes; parameter*BSQ score interaction). In fact, statistical testing did not support a need for separate intercepts for females and males; however, these had already been fit in the analyses of somatic syndromes and anxiety and so they were fit here as well.

Figure 4 illustrates the results of the regression model in which prevalence rates of the various insomnia parameters increased with increasing BSQ score. The p values establish the statistical significance of the BSQ score as a predictor of prevalence for each insomnia parameter. Overall, the BSQ score was a highly significant predictor of insomnia ($p < 0.0001$), driven by highly statistically significant p values for the impact of BSQ on the three insomnia frequency questions. Use of hypnotics approached but did not achieve statistical significance.

Discussion

The objective of this study was to determine whether increased BSQ score among SDB patients correlates with increased presence of somatic syndromes, anxiety, and insomnia. In our SDB population, we found that with increasing BSQ score, the prevalence of somatic syndromes, anxiety, and insomnia increased and the number of somatic syndromes per patient increased. In the remainder of this discussion, we consider how our findings can help to explain observations made in the SDB population.

Sex differences in the symptoms of OSA/H have been widely reported. Several studies have found that females with OSA/H complain more often of RLS [19], depression [19, 28, 29], anxiety [29], nightmares [19], insomnia [19, 28], and somatic syndromes [28] compared to males with OSA/H. We found that female sex raised the BSQ score by 5 to 6 points among SDB patients, raising the prevalence of somatic syndromes, anxiety, and insomnia among females. In addition, the prevalence rate of somatic syndromes and anxiety disorders was higher for females than for males at any BSQ score, magnifying the effect of the increased level of somatic arousal among females (Tables 2 and 4; Figs. 2 and 3). These disparities between the sexes are not explained by our findings.

Earlier studies have demonstrated that nasal CPAP treatment decreases the symptoms of fibromyalgia [11], RLS

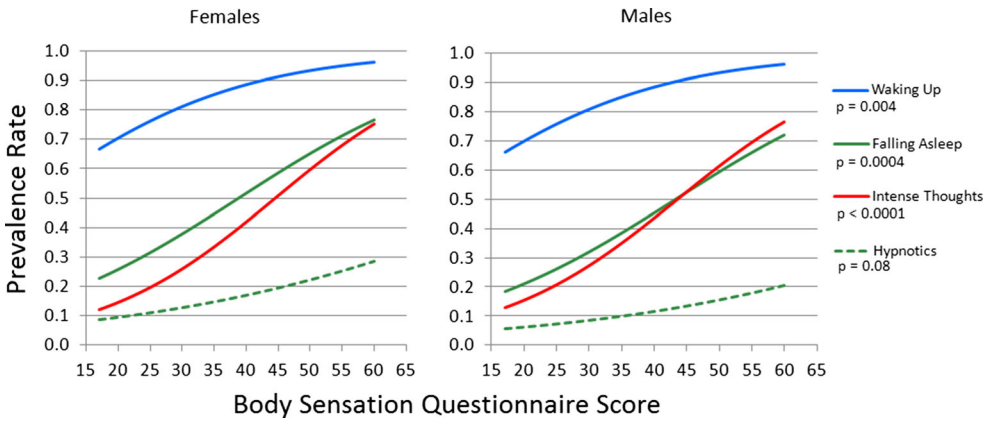

Fig. 4 The results of the regression model relating prevalence rates of the four insomnia parameters to increasing BSQ score for females and males with sleep disordered breathing. The p values for each parameter reflect the statistical significance of the correlation between prevalence rate and BSQ score for the combined samples (females and males). *Waking Up* wakes up during the night (sleep maintenance), *Falling Asleep* has difficulty falling asleep (sleep onset), *Intense Thoughts* lies awake with intense thoughts (sleep onset), *Hypnotics* has a prescription for hypnotics. The figure is further explained in the text

[30], and Gulf War illness [13]. Findings from this study together with the longitudinal findings of this patient group [16] suggest a paradigm that could account for the effect of nasal CPAP upon the somatic syndromes. In the current investigation, the prevalence rate of somatic syndromes among SDB patients was strongly correlated with the level of somatic arousal as characterized by the BSQ score (Fig. 2). In our associated study of this population [16], BSQ scores in 94 SDB patients declined by 5 to 6 points from baseline after treatment with nasal CPAP; fatigue severity, a common symptom of the somatic syndromes, decreased proportionately. A pathophysiologic paradigm based on these findings views the somatic syndromes as consequences of chronic stress caused by SDB. Nasal CPAP treatment improves the symptoms of the somatic syndromes by removing the stressor.

In our study, the level of somatic arousal among SDB patients was strongly correlated with the prevalence rate of anxiety-related outcomes. This finding can explain several associations in the literature between SDB and anxiety disorders [14, 31, 32]. Furthermore, CPAP treatment has improved the severity of panic attacks among males with sleep apnea [33] and the frequency of nightmares in veterans with PTSD and sleep apnea [34]. Indeed, the immediate cause of nightmares may be the increased SNS tone reflected in the BSQ score. Blocking the SNS tone with the alpha-adrenergic blocking agent prazosin decreases the frequency/severity of nightmares in patients with anxiety disorders [35, 36]. The effect of CPAP upon panic attacks and PTSD [33, 34] is readily understood in light of the decrease in BSQ score observed among the patients in this series treated with nasal CPAP [16]. Thus, the paradigm that SDB can be a source of increasing stress leading to increasing prevalence rates of anxiety outcomes explains the many observed relationships between SDB and anxiety disorders.

In this study, the level of somatic arousal among SDB patients was strongly correlated with the prevalence rate of insomnia-related outcomes. This should come as no surprise. The *somatic arousal* we measure with a BSQ score is the same phenomenon as the *physiologic arousal* postulated by Bonnet and Arand to be responsible for primary insomnia [37]. Indeed, the finding in our associated work that nasal CPAP use decreases somatic arousal among SDB patients suggests that co-existing SDB and insomnia are not two separate disorders, but that insomnia results from the somatic arousal caused by SDB. Indeed, Krakow and associates have recently demonstrated the high prevalence of SDB among many chronic insomnia patients not previously thought to have SDB [15]. Our findings in this study suggest that nasal CPAP treatment would be suitable for the chronic insomnia patients studied by Krakow's group.

In addition to suggesting a mechanism by which SDB can lead to chronic insomnia, our findings also provide some perspective on the relationship between the level of somatic arousal and the type of insomnia experienced. Table 5 (also Fig. 4) demonstrates two different patterns relating insomnia complaints to the level of somatic arousal. One pattern exists for the complaints of an inability to fall asleep and lying awake with intense thoughts. These two complaints are found in 20–40 % of patients (males and females) at the lowest BSQ scores and increase to prevalence rates of 50 % or more at the highest BSQ scores. In contrast, waking up during the night is already at a prevalence rate of 75 % in patients with scores ranging from 17 to 25, i.e., reporting little somatic arousal (Table 5), and approaches 90 % at the highest BSQ scores. These two patterns relating somatic arousal to insomnia complaints are consistent with the hypothesis that sleep-maintenance insomnia is a response to lower stress levels while sleep-onset insomnia is a response to higher stress levels.

Our analysis of this consecutive series of SDB patients has demonstrated that a higher BSQ score predicts higher prevalence rates of somatic syndromes, anxiety, and insomnia. Additionally, being female predicts higher prevalence rates of somatic syndromes and anxiety (but not insomnia). In an earlier study of 75 consecutive SDB patients, Gold and associates found that a lower AHI predicted a higher prevalence of sleep-onset insomnia, headache, IBS, and alpha-delta sleep [26]. Patients with UARS had higher prevalence of these symptoms and signs compared to patients with severe OSA/H even when females and males were considered separately [26]. The implications of somatic arousal were not considered in that work. Therefore, to extend the original result, we investigated the relationship of AHI to the prevalence of somatic syndromes, anxiety, and insomnia, controlling for sex and BSQ score, in the supplement to this paper (ESM 2). For fibromyalgia, CFS, and IBS, we found a significant incremental negative correlation between AHI and syndrome prevalence beyond the impacts of sex and BSQ score. For other somatic syndromes, anxiety, and insomnia, the correlations were not significant after adjusting for sex and BSQ score. We did not capture the presence of alpha-delta sleep in this study. Our supplemental findings suggest a modest incremental role for AHI as a determinant of the prevalence of somatic syndromes among SDB patients. Why UARS patients have higher rates of somatic syndromes compared to patients with severe OSA/H, even after adjustment for sex and BSQ score, remains uncertain.

Our finding that the prevalence of stress-related somatic syndromes, anxiety, and insomnia among SDB patients is correlated with the level of somatic arousal measured by self-report, alone, is intriguing. However, when our findings in this study are considered together with the associated observation that these patients' levels of both sleepiness and fatigue are also correlated with their levels of somatic arousal which decrease with treatment of their SDB, a new paradigm of SDB is suggested. This new paradigm extends beyond sleep fragmentation and hypoxemia caused by apneas and hypopneas resulting in sleepiness and fatigue. Rather, it suggests that

SDB (both UARS and OSA/H) activates the stress response leading to associated symptoms and syndromes.

Compliance with ethical standards

Funding No funding was received for this research.

Conflict of interest The authors declare that they have no competing interests.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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