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Subjective fatigue and subjective sleepiness: two independent consequences of sleep disorders?

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SUMMARY The objective of this investigation was to evaluate subjective fatigue versus subjective sleepiness as independent consequences of sleep disorders. Furthermore, we tried to explore how these symptoms relate to alertness, depressive symptoms and illness intrusiveness. In a prospective observational study, 283 sleep-disordered patients referred to a hospital-based sleep laboratory for various indications over a 1-year period were evaluated vis-à-vis fatigue and sleepiness. All patients completed five subjective questionnaires, underwent objective sleep recording and attended a clinical interview with a sleep specialist. The subjective questionnaires included the Epworth Sleepiness Scale, the Fatigue Severity Scale, the Toronto Hospital Alertness Test, the Illness Intrusiveness Rating Scale and the Center for Epidemiologic Studies-Depression Scale. Only 4% of the total sample was referred to the sleep clinic due to a complaint of excessive fatigue compared with 17% for excessive daytime sleepiness. However, during the assessment, 64% of referred patients reported pathological fatigue without overlap of sleepiness and only 4% reported pathological sleepiness without overlap of fatigue. Pearson's correlation analysis indicated a weak association ($r = 0.18$) between subjective fatigue and sleepiness in the total sample. Analysis of variance testing showed strong association between those patients with prominent fatigue and depressive symptoms ($P < 0.01$) and illness intrusiveness ($P < 0.001$). The findings support the notion that subjective fatigue and sleepiness can be independent manifestations of sleep disorders. Furthermore, predominantly fatigued individuals with sleep disorders seem vulnerable to additional negative consequences due to possible interplay between amplified fatigue and psychological distress.

KEYWORDS fatigue, sleep disorders, sleepiness, subjective rating scales

INTRODUCTION

The prevalence of fatigue in primary care patients is common and estimated to occur in 6–45% of patients (Cathebras *et al*., 1992; Godwin *et al*., 1999; Lee *et al*., 1991; Smets *et al*., 1995; Ward *et al*., 1996). This large range in prevalence is probably attributable to differences in the working definition of fatigue, measurement tools and the populations sampled. In comparison, excessive sleepiness ranges between 5 and 15% in the general population (Johns and Hocking, 1997; Ohayon *et al*., 1997; Partinen and Hublin, 2000; Roth and Roehrs, 1996). Although fatigue is a common incidental finding in a wide range of sleep disorders and has been documented in clinical reports, it has not been studied as an independent symptom in the context of sleep disorders. On the other hand, perceived excessive daytime sleepiness has gained universal recognition as a primary complaint of sleep clinic patients and an important public health concern (Roehrs *et al*., 2000).

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The terms 'sleepiness' and 'fatigue' are often used interchangeably by individuals undergoing sleep deprivation or sleep disruption (Dinges, 1995). Although fatigue does not seem to be identical with being sleepy, health care providers and patients tend to equate sleepiness with fatigue, probably due to overlap or coexistence of these symptoms in many physiological and pathological conditions (Shapiro and Kayumov, 2000). For example, sleepiness and fatigue both are associated with inactivity in many people. Although the two symptoms may occur together, these symptoms can also be dissociated. For example, fatigue but not sleepiness may occur after exercise, during pregnancy and in insomnia patients. Conversely, sleepiness but not fatigue is a problem in most narcoleptic patients (Abbey and Shapiro, 1995). Physiologically, sleepiness seems to be primarily dependent on the length of prior wakefulness and circadian rhythm status whereas fatigue depends on the level of exertion (Lichstein *et al*., 1997). A cross-association may also occur, i.e. prior wakefulness may effect fatigue and exertion effort may effect sleepiness. For example, inactivity or boredom may promote sleepiness and high exertion may produce increased wakefulness (Torsvall, 1981).

While occasional fatigue is a part of the strain of everyday life, persistent or frequent fatigue is often associated with conditions of physical or emotional illness and may be responsive to medical intervention (Belza, 1995; Lee *et al*., 1991). While some distinguish physiological fatigue from pathological fatigue by the inability of the latter to be relieved by rest, others simply view normal fatigue as being acute and pathological fatigue as chronic (Carpenito, 1995; Piper, 1989). Studies in experimental subjects with high fatigue scores demonstrate a lack of sustained physical functioning and difficulty meeting household responsibilities, compared with normal healthy individuals with low fatigue scores (Krupp *et al*., 1988; Wessely *et al*., 1996). However, fatigue continues to remain a poorly understood problem due to the absence of a 'gold-standard measuring tool' to assess non-specific fatigue and even fewer ways of managing and treating patients who complain of fatigue (Shapiro, 1998).

Sleepiness can be defined as being an awake-state in which an individual has an increased propensity to fall asleep (Dement, 1993). Excessive sleepiness can be conceptually defined as the desire or tendency to fall asleep at an inappropriate time, reflecting the 'ratio' of the total sleep-drive to the total wake-drive (Hanly and Shapiro, 1995; Johns, 1993). The concept of fatigue is more complex due to a wide range of interpretations that have been applied to it. Fatigue can be defined as being primarily a subjective experience that includes physiological performance decrements and psychological impairments such as decreased morale, judgment and mood (Brown, 1994). However, the physiological and psychological components have generally not been separately defined. Fatigue can also be defined with respect to its source as either work-related factors such as duration, timing, type of work or non-work-related factors such as general, medical, psychiatric and sleep disorders.

Although excessive sleepiness is regarded as one of the cardinal manifestations of sleep disorders and often is accompanied by fatigue, many patients with fatigue complain of insomnia and do not report falling asleep or feeling sleepy at inappropriate times (Aldrich, 2000). A wide range of sleep disorders can cause sleep deprivation and sleep disruption and are known to be contributory factors to excessive fatigue and/or sleepiness (Chesson *et al*., 2000; Hanly and Shapiro, 1995; Lichstein *et al*., 1997; Ohayon and Shapiro, 2000; Ward *et al*., 1996). A few studies have reported a high prevalence of potentially treatable primary sleep disorders among patients with chronic high fatigue (Buchwald *et al*., 1994; Krupp *et al*., 1993; Le Bon *et al*., 2000; Manu *et al*., 1994). Excessive fatigue as a daytime consequence has been reported in patients with chronic insomnia, the most common sleep complaint in primary health care settings (Chesson *et al*., 2000; Lichstein *et al*., 1997). In contrast, patients with chronic insomnia typically score in the normal range on subjective measures of daytime sleepiness (Johns, 1991; Lichstein *et al*., 1994; Olson *et al*., 1998).

A limited number of studies have investigated the relationship between sleepiness and fatigue in sleep-disordered patients such as obstructive sleep apnea (Aguillard *et al*., 1998; Chervin, 2000; Lichstein *et al*., 1997). These studies have generally demonstrated a poor agreement between the measures of fatigue and sleepiness and thus suggest that the two symptoms may have partial overlap but they are not identical phenomena and therefore require independent assessment. In our previous study, we have found a weak correlation between subjective fatigue and sleepiness rating in 195 shift-workers and also reported a significantly increased rate of primary sleep disorders (e.g. sleep apnea, periodic leg movements) in the subgroup of most-fatigued subjects when compared with least-fatigued shift-workers (Hossain *et al*., 2003).

Distinguishing between sleepiness and fatigue is important because etiology and treatment of these two states may differ. The relative dichotomy between sleepiness and fatigue and the under-emphasis of fatigue as an independent consequence of sleep disorders by many health professionals may have led to some patients with very treatable sleep disorders not being referred for sleep assessments. This may result in an underdiagnosis of sleep disorders, especially when fatigue rather than sleepiness is emphasized as the chief complaint to the primary care physicians. This observation may explain the high prevalence of undiagnosed sleep disorders among the middle-age population without obvious barriers to health care (Young *et al*., 1993, 1997, 2002). For example, it is estimated that among obstructive sleep apnea sufferers, as many as 93% of women and 82% of men with the disorder are undiagnosed (Young *et al*., 1997).

The primary objective of this investigation was to explore subjective fatigue versus sleepiness as independent manifestations of sleep disorders in a clinical population. The secondary objective was to assess how sleepiness and fatigue relate to alertness, depressive symptoms and illness intrusiveness in patients with sleep disorders. An exploratory objective was to

consider hypothetical constructs for pathogenesis and mechanism of fatigue and sleepiness in sleep-disordered patients in view of the findings of this study.

METHODS

This was a prospective observational study conducted in a group of sleep-disordered patients who were referred to the Sleep Clinic at the Toronto Western Hospital for various indications over a 1-year period. Ethics approval was obtained from the University Health Network Research Ethics Board before commencing the study. A total of 283 patients were selected from a pool of 1200 patients who were screened by the following inclusion and exclusion criteria:

The inclusion criteria: More than 14 years of age; referred by a community physician and had a specific indication for sleep study; completed five subjective questionnaires at the sleep laboratory; underwent polysomnography; and attended a clinical interview with a sleep specialist.

The exclusion criteria: Any prior diagnoses of medical disorders that may cause incremental fatigue or sleepiness; any medication or substances that would have influenced subjective fatigue or sleepiness; and subjects who did not meet the inclusion criteria.

Assessment and diagnoses of different sleep disorders was based on the International Classification of Sleep Disorders (ICSD) [American Sleep Disorders Association (ASDA), 1997], formulated from the clinical history provided by the patients in a consultation with a sleep specialist, sleep diary and detailed questionnaire and polysomnography. The subjects also completed the following questionnaires: the Epworth Sleepiness Scale (ESS), the Fatigue Severity Scale (FSS), the Toronto Hospital Alertness Test (THAT), the Illness Intrusiveness Rating Scale (IIRS) and the Center for Epidemiologic Studies-Depression (CES-D) Scale.

The ESS is a self-report questionnaire, which assesses subjective sleepiness and relies on dozing behavior in eight different situations of varying soporific nature (Johns, 1991). The questionnaire asks the respondent to rate the likelihood of falling asleep on a scale from 0 to 3, were '0' indicates no chance and '3' represents a great chance of dozing. Total ESS score is the sum of all the responses and ranges from 0 to 24, with higher scores reflecting greater sleep propensity. Consistent with the reports of a number of previous investigations, we adopted a score of 10 as the cut-off point for normal, above which implied pathological sleepiness (Chervin *et al*., 1997; Furuta *et al*., 1999; Johns, 1991, 1994; Olson *et al*., 1998; Sauter *et al*., 2000).

The FSS (Krupp *et al*., 1989) is a nine-item self-report questionnaire that assesses the degree of fatigue intensity on various functional and behavioral aspects of life and provides a subjective measurement of daytime fatigue that is largely independent of daytime sleepiness and depression. Each item is rated from 1 (strongly disagree) to 7 (strongly agree). Scoring of the FSS involves calculating the mean score for all statements. The range of possible scores is 1–7, with higher scores reflecting greater fatigue. The FSS provides an adequate means of assessing fatigue intensity within a general population, has high internal consistency, strong validation data and clearly distinguishes between patients and controls (Taylor *et al*., 2000). Consistent with the reports of a number of previous investigations, we adopted 3 being the cut-off point for normal, above which implied pathological fatigue (Aguillard *et al*., 1998; Herlofson and Larsen, 2002; Hossain *et al*., 2003; Krupp *et al*., 1989, 1993; Lichstein *et al*., 1997; Schwartz *et al*., 1993).

The THAT (C. M. Shapiro, C. Auch, M. Reimer, L. Kayumov, R. Heslegrave, N. Huterer, H. Driver, G. M. Devins, unpublished data) is a new approach to the construct of subjective alertness that assesses a range of activities such as: ability to concentrate; think of new ideas or focusing on the task on hand. THAT is a 10-item self-report questionnaire designed to measure perceived alertness in the preceding week. The respondent rates 10 different features of alertness on a scale of 0 (not at all) to 5 (all the time I was awake). Two items are worded negatively in order to disrupt the tendency toward a response set and need to be inverted during scoring. Possible score ranges from 0 to 50 and higher scores indicate a higher level of alertness and functioning. The interpretation and clinical utility of the scale at present has limitations due to unavailable validity and reliability information.

The IIRS is a self-report instrument, measuring the extent to which one's illness and/or its treatment 'interfere' with 13 life domains, important to one's quality of life (Devins *et al*., 1983). Each item is rated from 1 (not very much) to 7 (very much). The range of possible scores is 13–91 and higher scores reflect greater illness intrusion. Previous studies of different populations, which utilized the IIRS have reported it to be meaningful, reliable and valid measure of the extent of a given illness interfering with important life domains (Antony *et al*., 1998; Devins *et al*., 1983, 2001).

The CES-D is a 20-item self-report, four-point Likert scale (response range 0–3) developed to screen for cognitive/affective symptoms of depression in primary health care settings (Radloff, 1977). The components include depressed mood, feelings of guilt, helplessness, worthlessness, loss of appetite, psychomotor retardation and sleep disturbance. Four items are worded in a positive direction in order to disrupt the tendency towards a response set. The total scores can range from 0 to 60 and a score of greater than 16 indicates a clinically significant level of depressive symptoms (Radloff, 1977; Unutzer *et al*., 2002). The CES-D has been used in sleep-disordered populations and has been found to be a useful symptom scale to measure depression (Bardwell *et al*., 1999, 2000, 2003).

SELECTION CRITERIA FOR POSSIBLE OVERLAP OF FATIGUE AND SLEEPINESS

Association or dissociation of subjective fatigue and sleepiness was determined by the following criteria: (a) literature derived cut-off points for normal and pathological scores of the ESS and FSS rating scales; (b) mean subjective scores of sleepiness and fatigue in sleep-disordered patients of this sample; and (c)

various combinations of normal (low) and pathological (high) scores of sleepiness and fatigue in this sample.

The data were analyzed by using the Statistical Package for Social Sciences (SPSS) 11.5 version. One-way analysis of variance (ANOVA) was utilized to detect the significance of different subjective symptom scores among the four unique groups of overlap between fatigue and sleepiness, various diagnostic categories and between males and females. Tukey *post-hoc* multiple comparisons were carried out to determine which mean scores differed among the categories and the possibility of type-1 errors was minimized by Bonferroni's correction. The relationship between all the subjective measures from the total subject pool was examined by Pearson's correlation. Chi-square and Fisher's exact tests were carried out to differentiate the proportion of primary sleep pathology in the four unique groups as well as between males and females. Multiple regression testing was used to predict relationships between fatigue and sleepiness severity and various independent sleep variables.

RESULTS

The final sample included 283 patients, consisted of 161 males (56.9%) and 122 females (43.1%). The sample included 37 symptomatic patients on continuous positive airway pressure (CPAP) therapy who were referred to be assessed for a co-morbid disorder producing the symptoms (fatigue and/or sleepiness), notwithstanding adequate control of obstructive sleep apnea syndrome. The mean age of the sample was 45.2 ± 15.1 (SD) and the mean body mass index (BMI) was 28.8 ± 8.1 (SD).

According to the selection criteria, we categorized all the subjects into four distinct groups, as shown in Fig. 1.

Of the total sample, only 11 (4%) of the patients were primarily referred by their physicians for excessive fatigue complaint. However, based on the FSS, 181 (64%) of patients in the study group reported pathological fatigue without overlap of sleepiness. In contrast, 48 (17%) of the patient were referred due to an excessive sleepiness complaint, and only 11 (4%) reported pathological sleepiness without overlap of fatigue. Fig. 1 shows frequency of the four groups of overlap between fatigue and sleepiness.

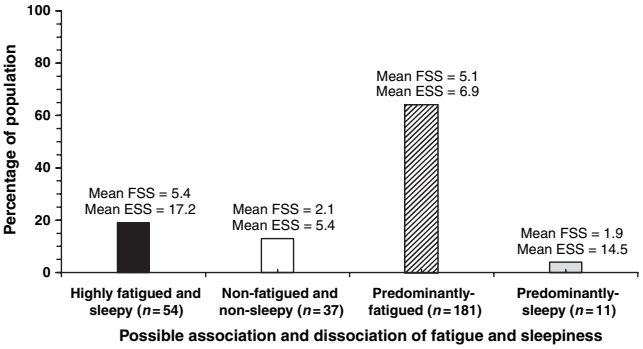

Figure 1. Frequency and percentage of the four groups in the sample ($n = 283$).

ANOVA testing showed significant differences in all the subjective measures between the four unique groups as shown in Table 1. Tukey *post-hoc* multiple comparisons revealed a significant difference in the illness intrusiveness score between predominantly fatigued (high fatigue/low sleepiness) and predominantly sleepy (high sleepiness/low fatigue) groups ($P < 0.01$). It also showed a significant difference in alertness and depression scores between high fatigue/high sleepiness (pathological overlap) and low fatigue/low sleepiness (normal overlap) groups ($P < 0.01$) and between predominantly fatigued (high fatigue/low sleepiness) and low fatigue/low sleepiness (normal overlap) groups ($P < 0.01$).

Statistical relationships between all the subjective measures from the total subject pool ($n = 283$) were examined in several ways including correlations, plots and frequency tables. Pearson's product–moment correlation analysis showed a non-significant association between continuous variables of subjective fatigue and sleepiness in this sample ($r = 0.18$). Moreover, a negative correlation was found between sleepiness and alertness ($r = -0.22$) and between fatigue and alertness ($r = -0.38$). To appreciate the strength and significance of the correlation analyses, the model summary of the measured variables are provided: subjective fatigue and sleepiness [$F(1,281) = 2.60$, $P < 0.284$]; subjective sleepiness and alertness [$F(1,281) = 3.38$, $P < 0.142$]; and subjective fatigue and alertness [$F(1,281) = 5.33$, $P < 0.036$].

Table 1 Mean (±SD) symptom scores in the four unique groups

	High fatigue/ low sleepiness	*High fatigue/ high sleepiness*	*Low fatigue/ low sleepiness*	*Low fatigue/ high sleepiness*	*Significance*
Age	45.0 ± 15.0	43.0 ± 14.0	48.2 ± 16.8	50.2 ± 13.6	NS
BMI	28.1 ± 6.7	31.5 ± 11.7	27.6 ± 7.6	30.7 ± 6.7	$F(3,279) = 3.0$, $P < 0.03$
ESS Score	6.9 ± 3.8	17.2 ± 2.7	5.4 ± 2.8	14.5 ± 2.9	$F(3,279) = 138.5$, $P < 0.0001$
FSS Score	5.1 ± 0.9	5.4 ± 1.0	2.1 ± 0.7	1.9 ± 0.6	$F(3,279) = 143.0$, $P < 0.0001$
CES-D Score	21.7 ± 11.0	23.0 ± 11.9	13.2 ± 10.6	19.4 ± 11.2	$F(3,279) = 6.86$, $P < 0.001$*
THAT Score	26.3 ± 8.0	23.12 ± 6.8	32.7 ± 9.5	25.0 ± 12.0	$F(3,279) = 10.35$, $P < 0.001$*
IIRS Score	42.1 ± 16.6	49.9 ± 17.3	23.9 ± 10.5	30.4 ± 15.0	$F(3,279) = 21.0$, $P < 0.0001$*

BMI, body mass index; ESS, Epworth Sleepiness Scale; FSS, Fatigue Severity Scale; CES-D, Center for Epidemiologic Studies-Depression; THAT, Toronto Hospital Alertness Test; IIRS, Illness Intrusiveness Rating Scale. *Tukey *post-hoc* multiple comparison test.

The frequency and percentage of primary sleep pathology and pathological symptom scores in the four unique groups are shown in Table 2.

Chi-square test showed that the predominantly fatigued (high fatigue/low sleepiness) patients had more than twice the illness intrusiveness score when compared with the predominantly sleepy (high sleepiness/low fatigue) patients ($P < 0.001$). The frequency of the different diagnostic categories and their mean subjective symptom scores are shown in Table 3.

Multiple regression analysis was utilized to predict the relationships between subjective fatigue and sleepiness severity (dependent variables) and the following independent variables: apnea–hypopnea index (AHI), periodic leg movements index (PLMI), arousal index and oxygen desaturation. ANOVA and Pearson's correlation were used to test the significance of the associations and most tests showed non-significant relationships between the symptoms and possible predictors. We also considered other potentially confounding factors such as age, gender and BMI. Factorial ANOVA within the regression analyses was utilized to measure the strength and significance of the observed relationships and that showed significant association between subjective sleepiness severity and BMI [$F(1,281) = 10.92$, $P < 0.001$] as well as subjective fatigue and gender [$F(1,281) = 12.41$, $P < 0.001$].

ANOVA testing detected significant differences between males and females as shown in Table 4. Female patients were found to be younger, had significantly higher fatigue, depressive symptoms and a lower alertness scores. Significantly more male patients (75.0%) were diagnosed with primary sleep disorders when compared with females (59%). Based on the Fisher's exact test, the difference in proportion of primary sleep pathology between the two groups was significant ($P < 0.005$).

DISCUSSION

The results of this study showed several new and interesting findings. Only a small percentage of the patients were referred

Table 2 Frequency of primary sleep disorders and pathological symptom scores

	High fatigue/ low sleepiness (n = 181)	*High fatigue/ high sleepiness (n = 54)*	*Low fatigue/ low sleepiness (n = 37)*	*Low fatigue/ high sleepiness (n = 11)*
Primary sleep disorders	114 (63)	42 (78)	26 (70)	9 (82)
Pathological subjective scores				
Depression	72 (68)	37 (69)	12 (33)	7 (64)
Illness intrusiveness	119 (66)	54 (100)	5 (14)	3 (27)
Alertness	163 (90)	43 (80)	21 (57)	9 (81)

Values in parentheses are in percentage.

Table 3 Mean (±SD) symptom scores in the major diagnostic categories

	FSS Score	*ESS Score*	*THAT Score*	*CES-D Score*	*IIRS Score*
Obstructive sleep apnea ($n = 93$)	4.4 ± 1.6	9.8 ± 5.6	28.6 ± 8.8	18.9 ± 12.5	39.2 ± 20.8
Periodic leg movements ($n = 33$)	4.6 ± 1.4	8.7 ± 5.5	27.0 ± 7.8	20.6 ± 12.5	39.9 ± 15.1
Restless legs syndrome ($n = 12$)	5.1 ± 1.0	11.9 ± 7.3	24.3 ± 6.3	18.4 ± 11.7	39.1 ± 17.3
Insomnia ($n = 33$)	4.4 ± 1.5	7.6 ± 5.2	28.0 ± 9.1	16.8 ± 8.5	39.4 ± 16.8
Depression ($n = 58$)	4.9 ± 1.4	7.7 ± 4.6	24.0 ± 8.5	27.0 ± 10.5	43.9 ± 17.4
Narcolepsy ($n = 9$)	4.8 ± 1.2	16.2 ± 3.5	21.5 ± 6.2	15.8 ± 7.3	39.4 ± 14.6
Parasomnia ($n = 11$)	5.2 ± 1.2	9.3 ± 6.2	21.5 ± 7.1	29.4 ± 5.6	44.3 ± 18.2
Delayed sleep phase syndrome($n = 15$)	4.6 ± 1.6	7.0 ± 5.6	25.4 ± 7.8	19.0 ± 9.9	35.3 ± 16.9

FSS, Fatigue Severity Scale; ESS, Epworth Sleepiness Scale; THAT, Toronto Hospital Alertness Test; CES-D, Center for Epidemiologic Studies-Depression; IIRS, Illness Intrusiveness Rating Scale.

Table 4 Mean (±SD) symptom scores in males and females

Subjective measures	*Male (n = 161)*	*Female (n = 122)*	*Significance*
Age	47.2 ± 15.8	42.6 ± 13.7	$F(1,281) = 6.45$, $P < 0.01$
BMI	28.6 ± 6.3	29.0 ± 10.0	NS
FSS Score	4.5 ± 1.5	4.9 ± 1.5	$F(1,281) = 6.0$, $P < 0.01$
ESS Score	9.4 ± 5.3	8.4 ± 5.8	NS
CES-D Score	18.4 ± 10.9	23.8 ± 11.6	$F(1,281) = 15.9$, $P < 0.001$
THAT Score	27.6 ± 8.7	24.9 ± 8.2	$F(1,281) = 6.8$, $P < 0.01$
IIRS Score	39.6 ± 18.3	42.3 ± 17.0	NS

BMI, body mass index; ESS, Epworth Sleepiness Scale; FSS, Fatigue Severity Scale; CES-D, Center for Epidemiologic Studies-Depression; THAT, Toronto Hospital Alertness Test; IIRS, Illness Intrusiveness Rating Scale.

to the sleep clinic due to excessive fatigue complaint compared with excessive sleepiness. However, data from self-reported subjective measures of sleepiness and fatigue showed a very different patient profile as defined by the four distinct categories of overlap between fatigue and sleepiness. During assessment, an overwhelming majority of the sample reported pathological fatigue without overlap of sleepiness and only a small number reported pathological sleepiness without overlap of fatigue. Moreover, correlation analyses indicated only a weak association between the symptoms of fatigue and sleepiness. We appreciate that subjective fatigue and sleepiness may have partial overlap but clearly these are not identical phenomena. A small number of previous studies also reported weak association between subjective sleepiness and fatigue in sleep-disordered patients in general and obstructive sleep apnea in particular (Aguillard *et al*., 1998; Chervin, 2000; Hossain *et al*., 2003; Lichstein *et al*., 1997). Our findings support the hypothesis that excessive sleepiness or fatigue can be independent consequences of sleep disorders.

Moreover, chi-square test showed a significant positive association between the patients with pathological fatigue and depressive symptoms and illness intrusiveness. In contrast, patients with pathological sleepiness yielded low illness intrusiveness scores. This suggests that a patient's illness experience may be influenced by the possible interplay between amplified fatigue and psychological distress and these factors may ultimately determine illness-related quality of life.

We found a closer negative association between subjective fatigue and alertness than that between subjective sleepiness and alertness in the total sample. Although limited by the unavailable validity and reliability data, this closer association may suggest that the alertness measure (THAT) may assess the opposite of fatigue rather than sleepiness. It is important to compare subjective alertness with sleepiness and fatigue because these three energy states are often used interchangeably in clinical medicine and may lead to misdiagnoses and inappropriate treatment (Shapiro and Kayumov, 2000).

We measured the significance of different subjective symptom scores among major diagnostic categories. Subjective sleepiness scores were very high and alertness scores were low in narcolepsy, which is consistent with the negative correlation found between these two measures in the total sample. Insomnia patients had normal subjective sleepiness but reported severe fatigue. This finding is in support of a number of previous studies and again emphasizes the dissociation of sleepiness and fatigue (Chesson *et al*., 2000; Johns, 1991; Lichstein *et al*., 1994, 1997; Olson *et al*., 1998).

Our sample showed significant differences in subjective measures between males and females. Female patients were found to have significantly higher fatigue, depressive symptoms and lower alertness scores despite their younger age and lower proportion with definitive sleep pathology. It seems plausible that the discrepancies between females and males may reflect difference in their perception of fatigue, alertness and depression.

Pathogenesis of fatigue and sleepiness in patients with obstructive sleep apnea syndrome and periodic limb movements disorder was explored. Oxygen desaturation and/or arousal-associated sleep fragmentation are generally acknowledged the clinical consequences of sleep apnea and implicated as a cause of fatigue and/or sleepiness. However, the lack of association between the subjective symptoms and suspected predictors suggests that increased fatigue or sleepiness severity may be produced by other factors. This is consistent with previous observations (Aguillard *et al*., 1998; Chervin, 2000; Chervin and Aldrich, 1999; Hossain *et al*., 2003). We also explored other confounding factors and found significant relationships between increased BMI and subjective sleepiness severity and between female gender and increased subjective fatigue. These findings suggest that multiple factors are associated with the subjective experience of fatigue and sleepiness.

The definition, etiology and pathogenesis of fatigue remain controversial and elusive. Sleep disorders and psychiatric illnesses are considered important correlates of fatigue and they interface in numerous ways. Most psychiatric patients have sleep complaints and many sleep-disordered patients have psychological complaints. The assessment of sleep and wake-related disorders affecting the sleep continuity and psychiatric co-morbidity are important factors in fatigue management (Bultmann *et al*., 2002; Ford and Kamerow, 1989). Some studies have reported that there is an inter-relationship between the causes and consequences of sleep disturbance and psychiatric illness in general and depression in particular (Baran and Richert, 2003; Breslau *et al*., 1996; Livingston *et al*., 1993; Shapiro, 2000). Therefore, the success or failure of treatment of fatigue or sleepiness can be strongly influenced by expertise in treating the primary and/or secondary sleep/psychiatric disorders. A number of studies have shown evidence of psychiatric co-morbidity as a manifestation of primary sleep disorders, particularly obstructive sleep apnea (Bardwell *et al*., 1999, 2000) and reversal of the symptoms after appropriate therapy (Means *et al*., 2003; Millman *et al*., 1989).

A recent study has demonstrated that excessive fatigue in obstructive sleep apnea patients may be strongly influenced by depressive symptoms and not apnea severity (Bardwell *et al*., 2003). Indeed, in our sample of 37 symptomatic patients on CPAP therapy after apnea severity was controlled, 21 had (by self-report) a high fatigue score and eight of them had co-morbid depression. Therefore, it seems reasonable to suggest that depressive symptoms may account for a significant portion of the fatigue severity experienced by obstructive sleep apnea patients even after therapeutic control of sleep disruption and hypoxia associated with the primary sleep disorder.

The visible discordance between subjective measures of fatigue and sleepiness in this clinical population discredits the reliance on sleepiness alone to estimate the validity of complaints of fatigue. These two symptoms can be distinct from each other in terms of individual perceptions and

pathophysiology, and are likely to require independent assessment in sleep-related and medical disorders. The discussion of relative discrepancy between subjective fatigue and sleepiness has been acknowledged in recent publications and valuable insights have been offered (Dement *et al*., 2003; Horne, 2003). The possibilities that may account for the relative incongruence between the subjective reports of sleepiness and fatigue as the consequences of sleep disorders and non-restorative sleep include: (a) subjective sleepiness due to neurophysiologic sleep drive may not be recognizable until it is substantial. In other words, individuals do not describe themselves as sleepy when the drive to sleep is mild or moderate. On the other hand, subjective fatigue may be experienced at the level of suboptimal or premorbid sleep drive and thus it seems to be a earlier indicator of increased need for sleep; (b) sleep-disordered individuals may not be able to identify increased sleepiness because of their chronic habituation to the symptom; (c) perception of sleepiness can be sufficiently masked or minimized by physical and mental conditions of high motivation, excitement and competing needs (e.g. hunger, thirst). In contrast, subjective fatigue is relatively unaffected by a stimulating environment; (d) persistent fatigue, even in absence of sleepiness, may be a manifestation of insufficient sleep or a sleep disorder. Female patients with sleep apnea are more likely to complain of fatigue, whereas males report more sleepiness (Redline and Strohl, 1998); (e) unwillingness of some individuals to describe the subjective state as being sleepy because of the general perception that increased need for sleep is a sign of personal weakness or lack of initiative. On the other hand, the description of being fatigued or tired seems more acceptable because it is perceived to be the result of hard work or effort.

Limitations of the present investigation need to be taken into account: (a) the observational study design provides only association, not causation of the measured variables; (b) sample size and selection bias within a sleep laboratory in a tertiary care hospital may not represent an adequately heterogeneous population; (c) no objective measure of sleepiness and fatigue were conducted to compare with the subjective symptoms; (d) relative discrepancy between the methodologies of the ESS (direct measure of sleep propensity by measuring sleepiness behavior) and the FSS (indirect measure of fatigue intensity by measuring functional impact of fatigue) may have influenced the results; (e) sample size of the subgroup of predominantly sleepy (low fatigue/high sleepiness) was small and that may have influenced the analyses and interpretation; (f) clinical outcome data of the various diagnostic categories were not considered within the scope of analyses and interpretation.

The findings of this study support the notion that subjective fatigue and sleepiness can be independent manifestations of sleep disorders and require independent assessment. Patients may experience either symptom as being more pronounced and may be able to only distinguish the most overwhelming symptom. Future investigations should address the limitations of the present study and establish a clearer separation of the role of sleepiness versus fatigue as the consequences of sleep disorders.

REFERENCES

Abbey, S. E. and Shapiro, C. M. Chronic fatigue syndrome and fibromyalgia. In: C. M. Shapiro (Ed.) *Sleep Solutions Manual*. Kommunicom Publications, Quebec, 1995: 148–167.

Aguillard, R. N., Riedel, B. W., Lichstein, K. L., Grieve, F. G., Johnson, C. T. and Noe, S. L. Daytime functioning in obstructive sleep apnea patients: exercise tolerance, subjective fatigue and sleepiness. *Appl. Psychophysiol. Biofeedback*, 1998, 23: 207–217.

Aldrich, M. S. Cardinal manifestations of sleep disorders. In: M. H. Kryger, T. Roth and W. C. Dement (Eds) *Principles and Practice of Sleep Medicine*, 3rd edn. W. B. Saunders Company, Philadelphia, 2000: 526–533.

American Sleep Disorders Association (ASDA). *International Classification of Sleep Disorders (ICSD)-revised edition*. Published by the American Sleep Disorders Association (ASDA). Davies Printing Company, Rochester, MN, USA, 1997.

Antony, M. M., Roth, D., Swinson, R. P., Huta, V. and Devins, G. M. Illness intrusiveness in individuals with panic disorder, obsessive-compulsive disorder, or social phobia. *J. Nerv. Ment. Dis*., 1998, 186: 311–315.

Baran, A. S. and Richert, A. C. Obstructive sleep apnea and depression. *CNS Spectr*., 2003, 8: 120–134.

Bardwell, W. A., Berry, C. C., Ancoli-Israel, S. and Dimsdale, J. E. Psychological correlates of sleep apnea. *J. Psychosom. Res*., 1999, 47: 583–596.

Bardwell, W. A., Moore, P., Ancoli-Israel, S. and Dimsdale, J. E. Does obstructive sleep apnea confound sleep architecture findings in subjects with depressive symptoms? *Biol. Psychiatry*, 2000, 48: 1001–1009.

Bardwell, W. A., Moore, P., Ancoli-Israel, S. and Dimsdale, J. E. Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity? *Am. J. Psychiatry*, 2003, 160: 350–355.

Belza, B. L. Comparison of self-reported fatigue in rheumatoid arthritis and controls. *J. Rheumatol*., 1995, 22: 639–643.

Breslau, N., Roth, T., Rosenthal, L. and Andreski, P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol. Psychiatry*, 1996, 39: 411–418.

Brown, I. D. Driver fatigue. *Hum. Factors*, 1994, 36: 298–314.

Buchwald, D., Pascualy, R., Bombardier, C. and Kith, P. Sleep disorders in patients with chronic fatigue. *Clin. Infect. Dis*., 1994, 18(Suppl. 1): 68–72.

Bultmann, U., Kant, I., Kasl, S. V., Beurskens, A. J. and Van Den Brandt, P. A. Fatigue and psychological distress in the working population: psychometrics, prevalence and correlates. *J. Psychosom. Res*., 2002, 52: 445–452.

Carpenito, L. J. *Nursing Diagnosis: Application to Clinical Practice*. J. B. Lippincott, Philadelphia, 1995: 379.

Cathebras, P. J., Robbins, J. M., Kirmayer, L. J. and Hayton, B. C. Fatigue in primary care: prevalence, psychiatric comorbidity, illness behavior and outcome. *J. Gen. Intern. Med*., 1992, 7: 276–286.

Chervin, R. D. Sleepiness, fatigue, tiredness and lack of energy in obstructive sleep apnea. *Chest*, 2000, 118: 372–379.

Chervin, R. D. and Aldrich, M. S. The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnea. *Neurology*, 1999, 52: 125–131.

Chervin, R. D., Aldrich, M. S., Pickett, R. and Guilleminault, C. Comparison of the results of the Epworth Sleepiness Scale and the Multiple Sleep Latency Test. *J. Psychosom. Res*., 1997, 42: 145–155.

Chesson, A., Hartse, K., Anderson, W. M., Davila, D., Johnson, S., Littner, M., Wise, M. and Rafecas, J. Practice parameters for evaluation of chronic insomnia. *Sleep*, 2000, 23: 237–241.

Dement, W. C. *Encyclopedia of Sleep and Dreaming*. Macmillan Publishing Company, New York, 1993: 554–559.

Dement, W. C., Hall, J. and Walsh, J. K. Tiredness versus sleepiness: semantics or a target for public education? *Sleep*, 2003, 26: 485–486.

Devins, G. M., Binik, Y. M., Hutchinson, T. A., Hollomby, D. J., Barre, P. E. and Guttmann, R. D. The emotional impact of end-stage renal disease: importance of patients' perception of intrusiveness and control. *Int. J. Psychiatry Med.*, 1983, 13: 327–343.

Devins, G. M., Dion, R., Pelletier, L. G., Shapiro, C. M., Abbey, S., Raiz, L. R., Binik, Y. M., McGowan, P., Kutner, N. G., Beanlands, H. and Edworthy, S. M. Structure of lifestyle disruptions in chronic disease: a confirmatory factor analysis of the Illness Intrusiveness Rating Scale. *Med. Care*, 2001, 39: 1097–1104.

Dinges, D. F. An overview of sleepiness and accidents. *J. Sleep Res.*, 1995, 4(Suppl. 2): 4–14.

Ford, D. E. and Kamerow, D. B. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? *JAMA*, 1989, 262: 1479–1484.

Furuta, H., Kaneda, R., Kosaka, K. et al. Epworth Sleepiness Scale and sleep studies in patients with obstructive sleep apnea syndrome. *Psychiatry Clin. Neurosci.*, 1999, 53: 301–302.

Godwin, M., Delva, D., Miller, K., Molson, J., Hobbs, N., MacDonald, S. and MacLeod, C. Investigating fatigue of less than 6 months duration: guidelines for family physicians. *Can. Family Physician*, 1999, 45: 373–379.

Hanly, P. J. and Shapiro, C. M. Excessive daytime sleepiness. In: C. M. Shapiro (Ed.) *Sleep Solutions Manual*. Kommunicom Publications, Quebec, 1995: 77–103.

Herlofson, K. and Larsen, J. P. Measuring fatigue in patients with Parkinson's disease – the Fatigue Severity Scale. *Eur. J. Neurol.*, 2002, 9: 595–600.

Horne, J. The semantics of sleepiness. *Sleep*, 2003, 26: 763.

Hossain, J. L., Reinish, L. W., Kayumov, L., Bhuiya, P. and Shapiro, C. M. Underlying sleep pathology may cause chronic high fatigue in shift-workers. *J. Sleep Res.*, 2003, 12: 223–230.

Johns, M. W. A new method of measuring daytime sleepiness; the Epworth Sleepiness Scale. *Sleep*, 1991, 14: 540–545.

Johns, M. W. Daytime sleepiness, snoring and obstructive sleep apnea. The Epworth Sleepiness Scale. *Chest*, 1993, 103: 30–36.

Johns, M. W. Sleepiness in different situations measured by the Epworth Sleepiness Scale. *Sleep*, 1994, 17: 703–710.

Johns, M. and Hocking, B. Daytime sleepiness and sleep habits of Australian workers. *Sleep*, 1997, 20: 844–849.

Krupp, L. B., Alvarez, L. A., Nicholas, G. L. and Scheinberg, L. C. Fatigue in multiple sclerosis. *Arch. Neurol.*, 1988, 45: 435–437.

Krupp, L. B., LaRocca, N. G., Muir-Nash, J. and Steinberg, A. D. The Fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch. Neurol.*, 1989, 46: 1121–1123.

Krupp, L. B., Jandorf, L., Coyle, P. K. and Mendelson, W. B. Sleep disturbance in chronic fatigue syndrome. *J. Psychosom. Res.*, 1993, 37: 325–331.

Le Bon, O., Fischler, B., Hoffman, G., Murphy, J. R., De Meirleir, K., Cluydts, R. and Pelc, I. How significant are primary sleep disorders and sleepiness in the chronic fatigue syndrome? *Sleep Res. Online*, 2000, 3: 43–48.

Lee, K. A., Hicks, G. and Nino-Murcia, G. Validity and reliability of a scale to assess fatigue. *Psychiatry Res.*, 1991, 36: 291–298.

Lichstein, K. L., Wilson, N. M., Noe, S. L., Aguillard, R. N. and Bellur, S. N. Daytime sleepiness in insomnia: behavioral, biological and subjective indices. *Sleep*, 1994, 17: 693–702.

Lichstein, K. L., Means, M. K., Noe, S. L. and Aguillard, R. N. Fatigue and sleep disorders. *Behav. Res. Ther.*, 1997, 35: 733–740.

Livingston, G., Blizard, B. and Mann, A. Does sleep disturbance predict depression in elderly people? *Br. J. Gen. Pract.*, 1993, 43: 445–448.

Manu, P., Lane, T. J., Matthews, D. A., Castriotta, R. J., Watson, R. K. and Abeles, M. Alpha-delta sleep in patients with a chief complaint of chronic fatigue. *South Med. J.*, 1994, 87: 465–470.

Means, M. K., Lichstein, K. L., Edinger, J. D., Taylor, D. J., Durrence, H. H., Husain, A. M., Aguillard, R. N. and Radtke, R. A. Changes in depressive symptoms after continuous positive airway pressure treatment for obstructive sleep apnea. *Sleep Breath.*, 2003, 7: 31–42.

Millman, R. P., Fogel, B. S., McNamara, M. E. and Carlisle, C. C. Depression as a manifestation of obstructive sleep apnea: reversal with nasal continuous positive airway pressure. *J. Clin. Psychiatry*, 1989, 50: 348–351.

Ohayon, M. M. and Shapiro, C. M. Sleep and fatigue. *Semin. Clin. Neuropsychiatry*, 2000, 5: 56–57.

Ohayon, M. M., Caulet, M., Philip, P., Guilleminault, C. and Priest, R. G. How sleep and mental disorders are related to complaints of daytime sleepiness. *Arch. Intern. Med.*, 1997, 157: 2645–2652.

Olson, L. G., Cole, M. F. and Ambrogetti, A. Correlations among Epworth Sleepiness Scale scores, multiple sleep latency tests and psychological symptoms. *J. Sleep Res.*, 1998, 7: 248–253.

Partinen, M. and Hublin, C. Epidemiology of sleep disorders. In: M. H. Kryger, T. Roth and W. C. Dement (Eds) *Principles and Practice of Sleep Medicine*, 3rd edn. W. B. Saunders Company, Philadelphia, 2000: 558–579.

Piper, B. F. Fatigue: current bases for practice. In: S. G. Funk, E. M. Tornquist, M. T. Champagne, L. A. Copp and R. A. Wiese. *Key Aspects of Comfort*. Springer, New York, 1989: 187–198.

Radloff, L. S. CES-D Scale: a self-report depression scale for research in the general population. *J. Appl. Psychol. Measurement*, 1977, 1: 385–401.

Redline, S. and Strohl, K. P. Recognition and consequences of obstructive sleep apnea hypopnea syndrome. *Clin. Chest Med.*, 1998; 19: 1–19.

Roehrs, T., Carskadon, M. A., Dement, W. C. and Roth, T.. Daytime sleepiness and alertness. In: M. H. Kryger, T. Roth and W. C. Dement (Eds) *Principles and Practice of Sleep Medicine*, 3rd edn. W. B. Saunders Company, Philadelphia, 2000: 43–52.

Roth, T. and Roehrs, T. A. Etiologies and sequelae of excessive daytime sleepiness. *Clin. Therap.*, 1996, 18: 562–576.

Sauter, C., Asenbaum, S., Popovic, R., Bauer, H., Lamm, C., Klosch, G. and Zeitlhofer, J. Excessive daytime sleepiness in patients suffering from different levels of obstructive sleep apnea syndrome. *J. Sleep Res.*, 2000, 9: 293–301.

Schwartz, J. E., Jandorf, L. and Krupp, L. B. The measurement of fatigue: a new instrument. *J. Psychosom. Res.*, 1993, 37: 753–762.

Shapiro, C. M. Fatigue: how many types and how common? *J. Psychosom. Res.*, 1998, 45: 1–3.

Shapiro, C. M. Sleep disruption as a cause and consequence of psychiatric illness. *Can. J. Diagn.* , 2000, November: 9–12.

Shapiro, C. M. and Kayumov, L. Sleepiness, fatigue and impaired alertness. *Semin. Clin. Neuropsychiatry*, 2000, 5: 2–5.

Smets, E. M. A., Garssen, B., Bonke, B. and De Haes, J. C. J. M. The multidimensional fatigue inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J. Psychosom. Res.*, 1995, 39: 315–325.

Taylor, R. R., Jason, L. A. and Torres, A. Fatigue rating scales: an empirical comparison. *Psychol. Med.*, 2000, 30: 849–856.

Torsvall, L. Sleep after exercise: a literature review. *J. Sports Med.*, 1981, 21: 218–225.

Unutzer, J., Patrick, D. L., Marmon, T., Simon, G. E. and Katon, W. J. Depressive symptoms and mortality in a prospective study of 2,558 older adults. *Am. J. Geriatr. Psychiatry*, 2002, 10: 521–530.

Ward, M. H., DeLisle, H., Shores, J. H., Slocum, P. C. and Foresman, B. H. Chronic fatigue complaints in primary care: incidence and diagnostic patterns. *J. Am. Osteopath. Assoc.*, 1996, 96: 34–46.

Wessely, S., Chalder, T., Hirsch, S., Wallace, P. and Wright, D. Psychological symptoms, somatic symptoms and psychiatric

disorder in chronic fatigue and chronic fatigue syndrome: a prospective study in the primary care setting. *Am. J. Psychiatry*, 1996, 153: 1050–1059.

Young, T., Palta, M., Dempsey, J., Skatrud, J., Weber, S. and Badr, S. The occurrence of sleep disordered breathing among middle-aged adults. *N. Engl. J. Med.*, 1993, 328: 1230–1235.

Young, T., Evans, L., Finn, L. and Palta, M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep*, 1997, 20: 705–706.

Young, T., Peppperd, P. E. and Gottlieb, D. J. Epidemiology of obstructive sleep apnea: a population health perspective. *Am. J. Respir. Crit. Care Med.*, 2002, 165: 1217–1239.