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Underlying sleep pathology may cause chronic high fatigue in shift-workers

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SUMMARY About 20–25% of the population in primary healthcare settings complains of chronic fatigue but this symptom has been under-emphasized compared with sleepiness in clinical practice. Shift-workers are particularly vulnerable because of various fatigue-related personal and public morbidity and mortality. The goal of this cross-sectional study was to explore if fatigue severity could be used as an independent predictive tool to identify underlying sleep pathology. The 21 most-fatigued (study group) and 23 least-fatigued (control) miners were selected on the basis of the Fatigue Severity Scale (FSS), which was administered to 195 subjects in an underground mine in Timmins, a town in northern Ontario. The two groups were matched for age, gender, and body mass index (BMI). Mean FSS score for the most-fatigued subjects was 4.9 ± 0.5 and the least-fatigued was 2.2 ± 0.5 ($P < 0.0001$). The subjects from each group were studied polysomnographically to identify sleep disorders. The polysomnographic data in 15 of 21 (71.4%) of the most-fatigued subjects displayed significant sleep pathology compared with only three of 23 (13.0%) in the least-fatigued subjects. Based on Fisher's exact test, the difference between the two groups was highly significant ($P < 0.0001$). Also, in the total subject pool ($n = 195$), the correlation between subjective fatigue and sleepiness was not very strong (Pearson's $r = 0.45$), suggesting that these two symptoms can be independent phenomena. It is concluded that chronic high fatigue can be an independent manifestation of underlying sleep pathology, which warrants independent subjective and objective assessment.

KEYWORDS fatigue, shift-work, sleepiness, sleep pathology

INTRODUCTION

Chronic fatigue is more prevalent in primary healthcare settings (20–25%) compared with excessive sleepiness (5–15%) but appears to be under-emphasized as an independent phenomenon because of apparent limitations in currently available psychometric tools to measure non-specific fatigue (Abbey and Shapiro 1995; Partinen and Hublin 2000; Shapiro 1998). There is a lack of consensus in the literature, regarding the definition of fatigue. In addition, there is no 'gold standard' measuring tool. Both of these factors make it all the more challenging for researchers and clinicians to investigate this ubiquitous phenomenon. To date, there is no clear demarcation between fatigue and sleepiness. Clinicians and investigators may equate fatigue with sleepiness because of the possible coexistence of these two symptoms but fatigue does not seem to be identical with being sleepy. While fatigue may be considered a state in which one's capacity or efficiency for work is reduced following physical or mental effort, it does not necessarily imply the irresistible desire for or tendency to fall asleep. In practice, these energy states are distinct feelings but there can be considerable overlap, and may produce similar results in some tests. For example, sleepiness and fatigue both may result in inactivity in most people, and both symptoms may occur together. However, these symptoms can also be

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dissociated, as evidenced in fatigue but not sleepiness after exercise, and sleepiness but not fatigue in most narcoleptic patients (Abbey and Shapiro 1995).

Although 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. Layzer (1990) identifies four types fatigue: (1) objective fatigue which refers to the inability to maintain a specified level of effort during exercise; (2) subjective fatigue which is a discomfort that suppresses the desire to pursue exercise; (3) systemic fatigue observed in athletes after a prolonged physical effort; and (4) asthenia, or neurasthenia, which refers to a complaint of general weakness, tiredness, or exhaustion without physiological abnormalities in the response to exercise, and frequently encountered in patients with sleep complaints. The first three types of fatigue are thought to have a neuromuscular origin whereas the fourth refers to a mental state. In summary, fatigue can be defined as a self-recognized state in which an individual experiences an overwhelming and sustained sense of exhaustion and decreased capacity for physical and mental work that is not relieved by rest (Aaronson *et al.* 1999; Carpenito 1995). Fatigue is difficult to define, not only because of its subjectivity in meaning and experience, but also because of its multidimensional, heterogeneous nature.

Distinguishing between sleepiness and fatigue is important because etiology and treatment may differ. The severity and duration of these symptoms are also important to be identified to explore the degree of their negative impact on quality of life. Etiology of fatigue and/or sleepiness can be broadly categorized into work-related and non-work related. Work-related fatigue and/or sleepiness occurs as a result of failure to achieve adequate restorative sleep. It results from cumulative effects of chronic and acute sleep deprivation and compounded by misalignment of a person's desired sleep–wake schedule and the output of the circadian pacemaker in the brain, inadequate sleep hygiene and increased duration of waking hours before beginning of work (Akerstedt 1987, 1988; Akerstedt *et al.* 2002; Czeisler and Shapiro 1995; Dawson and Fletcher 2001; Ohayon *et al.* 2002). Shift-workers are therefore particularly vulnerable and at increased risk of the consequences of increased sleepiness, chronic fatigue and decreased alertness and performance on/off the job an obvious detriment to their personal safety and that of their co-workers and society at large (Becker 1997; Heslegrave 1998).

Non-work related fatigue and/or sleepiness includes the impacts of sleep disorders, medical and psychiatric illnesses. Fatigue is a key symptom in a wide variety of medical and psychiatric disorders and it is often considered non-specific and therefore less-interesting aspect of any given illness. Fatigue in sleep-disordered individuals can be caused by sleep restriction or sleep disruption. Either or both may be caused by a broad range of sleep disorders, such as sleep apnea, periodic limb movement disorder, narcolepsy, psychophysiologic insomnia, circadian rhythm sleep disorders, chronic fatigue syndrome, fibromyalgia, alcohol and drug abuse, and psychiatric disorders (Abbey and Shapiro 1995; Hanly and Shapiro 1995; Lichstein *et al.* 1997; Ohayon and Shapiro 2000; Ward *et al.* 1996).

To date, there has been no objective measurement of sleep conducted in shift-workers selected on the basis of chronic fatigue severity to explore association between chronic high fatigue and underlying sleep pathology. This is an important research question as not all shift-workers from comparable demographics experience high fatigue. It is reasonable to postulate that, apart from the possible influence of shift-work itself, underlying sleep pathology may manifest in high fatigue by decreasing fatigue threshold in the affected individuals.

The primary objective of this study was to test whether there were differences in terms of underlying sleep pathology and sleep architecture between the most-fatigued (study group) and least-fatigued (control) shift-workers selected by subjective fatigue severity questionnaire. The specific aim was to detect if subjective fatigue severity could be used as an independent predictive tool to identify underlying sleep pathology in shift-workers. Secondary objective was to explore pathogenesis of fatigue severity and association between subjective fatigue and sleepiness. Exploratory objective was to compare daytime versus nighttime sleep in the 10-h shift-workers to explore possible influence of shift-work (time of the day) on output of polysomnography and sleep architecture.

If this approach of using fatigue as a predictor of sleep disorders as measured by the Fatigue Severity Scale (FSS) is successful, then the scale can be used in various industries as a low-cost screening tool to identify which high-risk individuals are likely to need sleep evaluation and subsequent medical treatment. It has enormous scope because in most cases, fatigue, associated with a sleep disorder can be easily and successfully treated if diagnosed propitiously and can significantly improve sleep and performance of the affected person.

METHODS

Two questionnaires *inter alia*, the Fatigue Severity Scale (Krupp *et al.* 1989) and the Epworth Sleepiness Scale (Johns 1991) were administered to 195 underground miners, working a 10-h shift schedule to assess their subjective fatigue and sleepiness. To experiment on an extreme range of fatigue experience, 23 most severely fatigued (study group) and 23 least-fatigued (control) miners were selected from the total subject pool based on the Fatigue Severity Scale (FSS) score only.

The Fatigue Severity Scale (FSS) is a nine-item self-reporting questionnaire emphasizing on functional and behavioral aspects of fatigue (Appendix 1), asking the respondent to choose a number from 1 to 7 for each statement of fatigue, where 1 indicates no impairment and 7 indicates severe impairment. The Fatigue Severity Scale represents adequate means of assessing fatigue intensity within general population, has high internal consistency, and clearly distinguishes between patients and controls (Taylor *et al.* 2000). The Epworth Sleepiness Scale (ESS) is a self-reporting questionnaire to assess subjective sleepiness and relies on dosing behavior in eight different situations of relatively low soporific nature, asking the respondent to rate the likelihood of falling asleep on a scale from 0 to 3, were 0 indicates no chance and 3 being the greatest chance of dosing. Its retrospective composite score captures much better sleepiness profile compared with any other available sleepiness scales. The ESS is reported to be the most discriminating test to quantify daytime sleepiness when compared with multiple sleep latency test (MSLT) and the maintenance of wakefulness test (MWT) (Johns 2000).

Mean FSS score for the severely fatigued subjects was 4.9 ± 0.5, and the least fatigued was 2.2 ± 0.5 ($P < 0.0001$). These two groups are shown in Fig. 1 in comparison with literature-derived normal controls and patients with fatigue illnesses as described below. To compare FSS score across samples, Krupp *et al.* (1989) reported 2.3 ± 0.7 in healthy adults, 4.7 ± 1.5 in systemic lupus erythematosis (SLE) and 4.8 ± 1.3 in multiple sclerosis (MS). Lichstein *et al.* (1997) reported an average of 4.8 FSS score among 206 subjects with broad range of sleep disorders. Aguillard *et al.* (1998) reported 4.8 ± 1.4 mean FSS score among a sample of 32 obstructive sleep apnea patients.

To be able to detect the particular influence of underlying sleep pathology to cause fatigue, all subjects were screened for any medical or psychiatric co-morbidity known to cause incremental fatigue and/or sleepiness. However, none of the subjects from either group had to be excluded as a result of any physical illness.

The subjects were working shift-work at the mine for an average of 15.2 ± 6.5 years and working 10-h shift schedule for 2 years. The two extreme groups were all men and closely matched for age (41.4 ± 6.5 years versus 42.2 ± 6.5 years) and body mass index or BMI (29.6 ± 4.4 kg m^{-2} versus 27.7 ± 2.9 kg m^{-2}).

Ethics approval and informed consent were obtained from all the subjects who underwent objective evaluation of sleep (polysomnography) conducted on two consecutive occasions to identify underlying sleep pathology and evaluate sleep

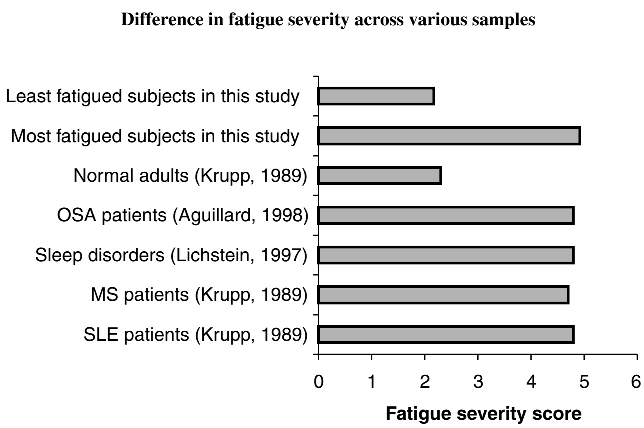

Figure 1. Fatigue assessment in different populations showing comparison between normal and various disorders known to be associated with subjective report of high fatigue.

architecture. The purpose of two consecutive sleep studies was to offer an adaptation period and minimize the 'first night effect', which is a physiological response in healthy individuals characterized by alteration of the sleep structure as a result of natural stressors, such as sleeping at an unfamiliar surroundings (Agnew *et al.* 1966). Two subjects from the most-fatigued group were excluded from the analyses because they participated in only one sleep study instead of two consecutive ones. Of the remaining 21 most-fatigued subjects, 11 had daytime and 10 had nighttime measurements. In the low-fatigue group, 14 subjects had daytime and nine had nighttime measurements. The aim of collecting daytime versus nighttime sleep was essential to explore influence of shift-work (time of the day) on output of polysomnography and sleep architecture that may affect fatigue.

Sleep study timing at the laboratory was based on their shift-work schedule and normal sleeping time. The shift schedules of the two groups were same before sleep recording. The 10-h shift schedule consisted of two shifts: day (19:00 hours to 17:00 hours) and night (17:00 hours to 03:00 hours). The miners worked a forward rotating schedule consisting of four consecutive day shifts followed by 2 days off and then three consecutive night shifts. After completing the night shift (03:00 hours), the subjects came directly to the sleep laboratory (by 04:00 hours) and were able to go to bed by habitual bedtime (05:00 hours) and were awaken by 14:00 hours. After completing day shift, subjects went to their homes and returned to the sleep laboratory by 20:00 hours and went to bed by 21:00 hours and awaken by 06:00 hours to be able to go to work by 07:00 hours.

The Stanford Sleepiness Scale (Hoddes *et al.* 1973) was administered to every subject of the two groups of contrasting fatigue severity to assess the degree of their sleepiness at the sleep laboratory. The Stanford Sleepiness Scale is a self-rating scale asking respondents to choose one of seven hierarchical statements that most closely describes their degree of sleepiness at a particular point in time. No significant difference was noted between the most- and least-fatigued groups (2.65 ± 0.93 versus 2.26 ± 0.96).

The subjects from each group were studied polysomnographically to identify underlying sleep pathology and evaluate sleep architecture. Sleep assessments were conducted at a temporary sleep laboratory in Timmins, equipped with Alice-3 computerized sleep acquisition system. The recording montage consisted of C3/A2 and C4/A1 electroencephalogram (EEG); right and left electro-oculogram (EOG); bipolar submental electromyogram (EMG); thoracic and abdominal piezoelectric bands; oronasal thermocouple to measure airflow; finger pulse oxymetry for oxygen saturation; bipolar electrocardiography (ECG) leads, bilateral anterior tibialis EMG; and mercury gauge body position sensor. Sensors were placed and equipment was calibrated during day/night sleep by a registered technologist. The recorded data were stored in real time in the computers, locally reviewed and then archived on to CDs to be forwarded to the Sleep Research Laboratory at the Toronto Western Hospital.

All the recorded data were blindly scored in accordance with universally acceptable scoring rules and guidelines (Rechtschaffen and Kales 1968; Shapiro and Rathouse 1990). Apart from detecting primary sleep pathology, other sleep measurements were identified, such as Modified Sleep Quality Scale (Table 1) and Sleep Fragmentation Scale (Table 2) to test differences between the two extreme groups. We have modified the 12-item Sleep Quality Scale (Huterer *et al.* 1996) by eliminating apnea index, apnea–hypopnea index (AHI), periodic limb movement (PLM) index and adding arousal index to obtain a more pure EEG effect on total sleep quality to measure severity of abnormal sleep architecture suggestive of non-restorative sleep. The underlying conceptualization of this scale is that sleep can be viewed as continuum of different components, and disruption of any component may contribute to a deterioration of sleep quality. Each item value of the scales range from 1 to 4, 1 being normal and higher scores quantifying progressively greater severity of sleep quality disruption, which may ultimately produce fatigue or sleepiness.

RESULTS

SPSS 10.1 statistical software was used for detailed analyses of sleep architecture and associated events to provide polysomnographic information concerning sleep disorders, blind to the fatigue level and address the primary, secondary and exploratory objectives of the study. Only the results of the second study were used for analyses as the first study was considered to be influenced by the 'first night effect'. Two subjects from the most fatigued group were excluded from the analyses because they participated in only one sleep study instead of two consecutive ones.

Primary outcomes

Consistent with the primary hypothesis, there was a extremely significant difference between the two groups ($P < 0.0001$) based on Fisher's exact test comparing the proportion of subjects with sleep pathology between the most- and least-fatigued groups. Fifteen of 21 (71.4%) of the severely fatigued subjects (study group) displayed significant sleep pathology and polysomnographic features of obstructive sleep apnea (11), periodic limb movements disorder (2), bruxism (1) and severe alpha–delta sleep (1). Compared with this, only three of 23 (13.0%) of the least-fatigued subjects (control) had evidence of sleep pathology in polysomnography such as sleep apnea (2) and periodic limb movements disorder (1).

ANOVA was used to test difference of various sleep measurements between the most and least-fatigued subjects as shown in Table 3. Overall, sleep quality score was much worse in the most-fatigued subjects compared with the least fatigued ($P < 0.001$). Moreover, severity of sleep apnea, measured by mean AHI was significantly higher in the most fatigued (10.2 per hour) versus least fatigued (2.6 per hour) subjects ($P < 0.05$).

Secondary outcomes

Multiple regression analysis (Stepwise and hierarchical) was used to predict relationship between fatigue severity (dependent variable) and the following independent variables: sleep

Table 1 Modified Sleep Quality Scale (SQS)

Points	*1 – Normal*	*2 – Mild disturbance*	*3 – Moderate disturbance*	*4 – Severe disturbance*
Total sleep time (h)	Young, 8; middle age, 7.2	± 1–2	± 2–3	± 3 or above
Sleep efficiency (%)	90–100	80–90	70–80	< 70
Sleep latency (min)	11–20	21–30	0–10	> 30
REM latency (min)	80–100	70–80 or 100–110	< 70 or > 110	> 120 or < 60
REM sleep (%)	Normal % for age	± 5	± 6–10	± 11–20
Slow-wave sleep (%)	Normal % for age	± 5	± 6–10	± 11–20
Stage 1 (%)	Normal % for age	± 5	± 6–10	+ or > 11
Oxygen saturation (%)	> 90	80–90	70–80	< 70
No. of awakening/total sleep time	< 5	5–10	11–20	> 20
Arousal index (per hour)	< 5	5–10	11–20	> 20

This set of values ranging from 1 to 4, 1 being normal and higher scores quantifying progressively greater severity of disruption of normal sleep architecture has been empirically derived.

Table 2 Sleep Fragmentation Scale (SFS)

Points	*1 – Normal*	*2 – Mild disturbance*	*3 – Moderate disturbance*	*4 – Severe disturbance*
Arousal index (per hour)	< 5	5–10	11–20	> 20
Number of awakenings (per TST)	< 5	5–10	11–20	> 20
Sleep-stage changes (per TST)	20–40	41–60	61–80	> 80

The features of sleep fragmentation has been derived from literature review.

Table 3 ANOVA testing of sleep structure differences between the most- and least-fatigued subjects

Variables	*Most fatigued ($n = 21$)*	*Least fatigued ($n = 23$)*
Sleep Quality Score*	2.85 ± 0.4	2.43 ± 0.4
Sleep Fragmentation Score	2.7 ± 0.7	2.8 ± 0.7
Time in bed (min)	351 ± 48.8	334 ± 5
Total sleep time (min)	303.3 ± 45.8	273.7 ± 55.2
Sleep efficiency (%)	88.0 ± 6.7	82.8 ± 10.5
Sleep latency (min)	13.5 ± 18.3	12.2 ± 12.0
REM latency (min)	104.5 ± 54.4	88.6 ± 43.0
REM sleep (%)	18.9 ± 6.7	18.9 ± 9.3
Stage 1 sleep (%)	6.5 ± 3.4	9.9 ± 6.3
Slow-wave sleep (%)	17.6 ± 7.8	11.5 ± 9.2
Arousal index (per hour)	13.9 ± 8.8	12.6 ± 6.7
Apnea hypopnea index (AHI)**	10.2 ± 15.6	2.6 ± 6.4

*$P < 0.001$; **$P < 0.05$.

pathology, AHI, PLM, oxygen desaturation, sleep quality score (SQS), sleep fragmentation score (SFS), arousal index and sleep study timing (day/night). ANOVA was used to test significance of difference of the variables. Both tests showed very significant relationship between the fatigue severity as dependent variable and sleep pathology as predictor ($P < 0.0001$). Again, stepwise multiple regression was performed to predict the relationship between sleep quality score (SQS) as dependent variable and the following independent variables: fatigue severity, sleep pathology and sleep study timing, which showed a significant relationship between SQS and sleep pathology as predictor ($P < 0.0001$). Moreover, there was strong evidence of a relationship between oxygen desaturation and fatigue severity according to chi-square test ($P < 0.001$). 92% of the subjects in high fatigue group had oxygen desaturation compared with only 31% of subjects in the low fatigue group. Interestingly, sleep study timing was found to be a significant predictor of periodic limb movements disorder in logistic regression analysis ($P < 0.01$). Of the subjects with PLMD, 80% were studied during nighttime and of those without PLMD, 68% were studied during daytime. These are very significant findings towards exploring the pathogenesis of fatigue as there was no significant relationship found between severity of fatigue and severity of sleep apnea (Pearson's $r = 0.33$) or periodic limb movements disorders (Pearson's $r = 0.16$).

The relationship between subjective sleepiness and fatigue using mean score of Epworth Sleepiness Scale and Fatigue Severity Scale data from total subject pool ($n = 195$) and the most- and least-fatigued group ($n = 46$) were examined in several ways including correlations, plots and frequency tables. The correlation between subjective sleepiness and fatigue in the total subject pool ($n = 195$) was not very strong (Pearson's $r = 0.45$), the relationship is plotted in Fig. 2. The mean independence between the categorized versions of the ESS and the FSS was tested by chi-square. Within the low ESS group ($n = 136$), 81% of the subjects were in the low FSS group, however within the high ESS group ($n = 59$), only 35% had high FSS.

Moreover, among the most- and least-fatigued subjects ($n = 44$), 17 subjects were in high fatigue/low sleepiness and six were in low fatigue/high sleepiness; 15 were in low fatigue/low sleepiness and six were high fatigue/high sleepiness categories. Fig. 3 shows the percentage of these four special groups with various levels of sleepiness and fatigue overlapping.

All these findings are consistent with the notion that subjective fatigue and sleepiness can be independent phenomena in association with sleep disorders.

Exploratory outcomes

The analysis included ANOVA to test the difference of various sleep measurements and their significance between daytime ($n = 25$) versus nighttime sleep ($n = 19$). Table 4 summarizes the ANOVA results of continuous exploratory outcomes where P-values are given for each effect tested. Objective sleep laboratory results showed 10-h day-shift workers (nighttime sleep) stayed in bed significantly longer, took longer time to fall asleep and slept longer than 10-h night-shift workers (daytime sleep). However, contrary to perceived influence of shift-work (time of the day) on output of polysomnography and sleep architecture, there was no significant difference of overall sleep quality score between daytime and nighttime sleep. There was no significant difference of mean AHI between daytime versus nighttime sleep (7.0/h versus 5.0/h). Moreover, as stated earlier in the secondary outcome regression analyses, sleep study timing was not found to be a predictor of sleep quality score or fatigue severity.

DISCUSSION

Highly significant difference in proportions of underlying sleep pathology between the most- and least-fatigued groups is consistent with the primary hypothesis to suggest that chronic high fatigue can be a considered as an independent manifestation of underlying sleep pathology. This indicates that patients presenting with fatigue should be evaluated vis-à-vis their sleepiness. This study has provided some evidence in support of chronic high fatigue being an independent phenomenon in sleep-disordered individuals.

We tried to construct an integrative tool to quantify overall sleep quality and sleep fragmentation, which has given us some directions towards detecting pathogenesis of fatigue. There was a significant difference between the most- and least-fatigued groups for sleep quality scale score. Multiple regression analysis showed very significant relationship between the fatigue severity as dependent variable and sleep pathology as predictor. It also showed a significant relationship between sleep quality score as dependent variable and sleep pathology as predictor. Moreover, oxygen desaturation showed a highly significant difference between the low- and high-fatigued subjects. Therefore, overall abnormality in sleep architecture measured by sleep quality scale or even an individual variable may contribute to pathogenesis of excessive fatigue. It is well

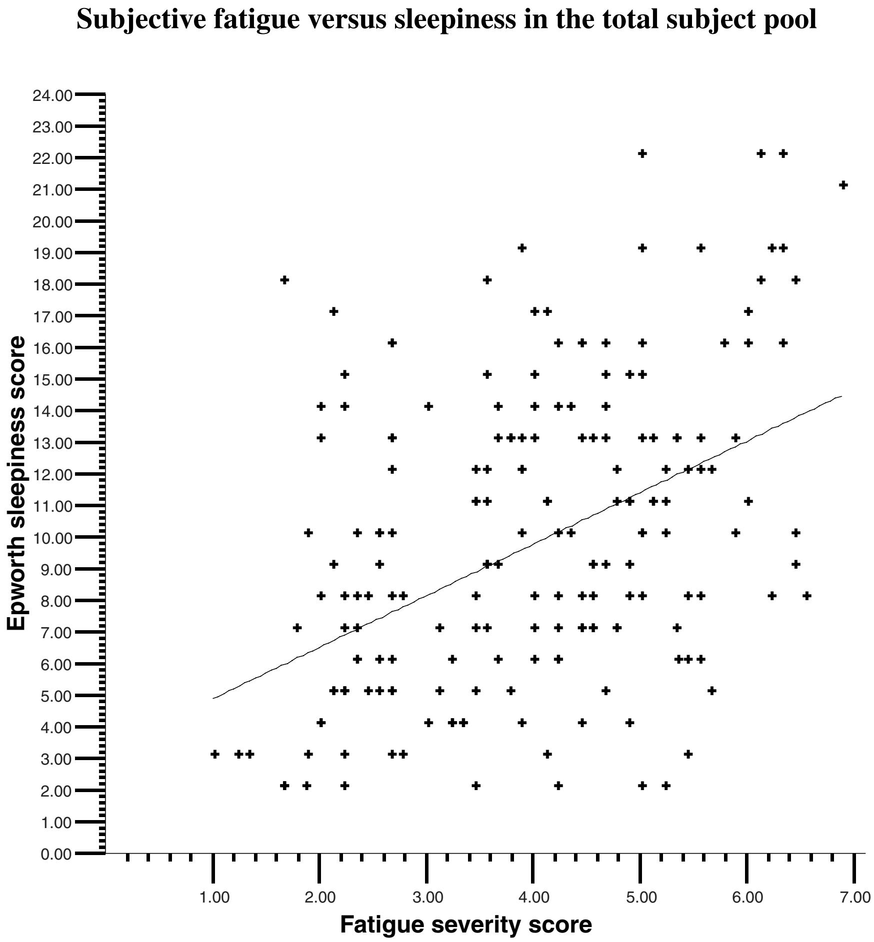

Figure 2. Correlation between the subjective fatigue and sleepiness scores in the total subject pool ($n = 195$) is shown in the scatter plot with the regression line (Pearson's $r = 0.45$).

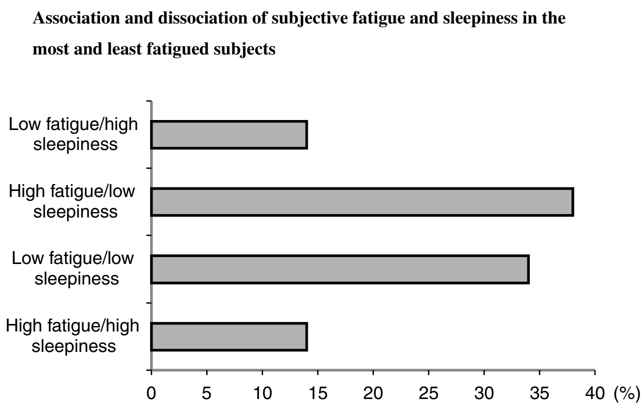

Figure 3. This figure shows the various permutation and combination of subjective sleepiness and fatigue dichotomized into high and low scores among the most- and least-fatigued subjects.

known that sleep apnea patients may present with two clinical consequences: either an arousal of some sort and/or oxygen desaturation. Consistent with the previous findings (Aguillard *et al.* 1998), apnea severity was not significantly correlated with subjective fatigue or sleepiness severity measured by the FSS or ESS score, suggesting that increased fatigue among apnea patients may be produced by factors other than apnea *per se*.

Table 4 ANOVA testing for differences between shift-workers sleeping during daytime and nighttime

Variables	*Daytime sleep (n = 25)*	*nighttime sleep (n = 19)*
Age	41.7 ± 6.2	41.8 ± 6.8
Body mass index	28.6 ± 3.4	28.5 ± 4.3
Sleep Quality Score	2.6 ± 0.4	2.7 ± 0.5
Sleep Fragmentation Score	2.6 ± 0.8	2.9 ± 0.6
Time in bed (min)*	314.2 ± 43.6	376.7 ± 35.4
Total sleep time (min)***	272.0 ± 56.1	306.8 ± 41.8
Sleep efficiency (%)	87.2 ± 8.7	83.0 ± 9.4
Sleep latency (min) **	6.8 ± 8.4	20.0 ± 18.3
REM latency (min)***	80.4 ± 38.8	115.0 ± 53.8
REM sleep (%)	20.9 ± 9.3	16.6 ± 5.6
Stage 1 sleep (%)	8.6 ± 6.4	7.9 ± 3.8
Slow-wave sleep (%)	16.0 ± 9.8	12.5 ± 7.8
Arousal index per hour	13.7 ± 8.7	12.6 ± 6.5
Apnea hypopnea index (AHI)	7.0 ± 13.9	5.0 ± 10.0

$^{*}P < 0.001$; $^{**}P < 0.003$; $^{***}P < 0.02$, $P < 0.03$.

Subjective fatigue and sleepiness did not correlate strongly in the total subject pool and the high-fatigued group, suggesting that patient's complaints of fatigue are not just a reference to excessive daytime sleepiness that accompanies underlying sleep disorders and abnormal sleep architecture. Instead, high subjective fatigue may refer to diminished physical ability in sleep-disordered patients, who are able to distinguish between sleepiness and fatigue as the presenting or overwhelming symptom. This may be interpreted as high-fatigued subjects can identify fatigue as an independent symptom and make the distinction from being sleepy. Surprisingly, none of the high-fatigued subjects showed any evidence of psychophysiological insomnia, one of the most common sleep disorders to produce chronic high fatigue. Perhaps, involvement of heavy manual labour and prolonged shift duration caused the miners to be physically exhausted before bedtime, which induced effortless sleep onset and maintenance.

Only a limited number of studies have investigated relationship between sleepiness and fatigue in sleep disordered patients (Aguillard *et al.* 1998; Chervin 2000; Lichstein *et al.* 1997). Previous evidence for the distinction between fatigue and sleepiness includes a 1997 study of fatigue in 206 sleep-disordered subjects, which found multiple sleep latency test (objective measure of sleepiness) had no predictive value of the fatigue score measured by the FSS (Lichstein *et al.* 1997). A 1998 study conducted in 32 sleep apnea patients found no significant correlation between objective testing for sleepiness and fatigue, suggesting that daytime sleepiness and daytime fatigue are independent problems (Aguillard *et al.* 1998). A questionnaire study conducted among 190 obstructive sleep apnea patients revealed that, when required to select the one most significant symptom, more patients chose fatigue (about 40%) than any other problem, including sleepiness (about 22%)(Chervin 2000). Another study compared subjective fatigue and sleepiness based on the FSS and the ESS among 199 normal and 96 hepatitis-C infected individuals. The correlation between fatigue and sleepiness rating within hepatitis-C patients and normal subjects were not strong, $r = 0.37$ and $r = 0.29$, respectively (H. S. Driver, N. Huterer, G. M. Devins, L. Kayumov, M. Sherman, M. P. McAndrews, D. Mikulis and C. M. Shapiro, unpublished data). This correlation indicates that it is far from the case that sleepiness and fatigue always run *pari pasu* but suggests that these symptoms are related but not identical. In addition, there is an increasing amount of evidence to suggest that central mechanisms involved in sleepiness may be distinct from those at play in fatigue (Lichstein *et al.* 1997; Sheean *et al.* 1997; Spierings and Van Hoof 1997). However, we need further evaluation to independently assess subjective and objective fatigue and sleepiness to draw a clear separation.

Fatigue Severity Scale seems to be a useful practical tool in differentiating between groups for severity of fatigue assessment. However, it may require further evaluation in a large longitudinally designed study. Moreover, the relationship between the subjective and objective measures of fatigue is not clear because of the non-specific nature of the available tools to quantify fatigue without overlapping with measures of sleepiness. This warrants further investigation to explore ubiquitous nature of fatigue and the possibility of fatigue being a key complaint of patients with primary sleep disorders and other common causes of chronic fatigue, such as chronic fatigue syndrome, fibromyalgia, and depression. A number of studies have reported relatively high prevalence of chronic fatigue in primary sleep disorders who are clinically distinguished from patients with a different etiology (Buchwald *et al.* 1994; Le Bon *et al.* 2000; Manu *et al.* 1994). Moreover, chronically fatigued patients with coexistent clinical conditions may require an intervention for a treatable cause of their fatigue and it is necessary to distinguish between various differential diagnoses.

Limitations of the present investigation should be taken into account. Firstly, non-random selection of the subjects was able to assess only association, not causation of fatigue in the two extreme groups. However, random assignment could have resulted in an unpredictable difference of fatigue level between the two groups because of a wide range of fatigue severity across the population. Second, subject selection was based on fatigue severity only, its overlap or separation from sleepiness was not evaluated to detect the better predictor. Third, objective measurement of sleepiness or fatigue was not conducted in the miners to evaluate their subjective complaints. Finally, sample size was small considering number of variables examined. The results in the primary outcome had 50% power in detecting a difference between the two extreme groups.

Future investigations should address the limitations and lead to a clearer separation of the role of sleepiness versus fatigue and ultimately identify which symptom expression is the better predictor of underlying sleep pathology. An analogous study conducted in a different population for subjective and objective evaluation sleep, fatigue, sleepiness, and performance would be desirable. Furthermore, conducting intervention study in the subjects with underlying sleep pathology will be critical for assessment of causality to test hypothesis.

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Appendix 1 The fatigue severity scale (FSS).
Circle a number from 1 to 7 that indicates your degree of agreement or disagreement with each item

	Strongly disagree			*Neither*		*Strongly agree*	
1. My motivation is lower when I am fatigued	1	2	3	4	5	6	7
2. Exercise brings on my fatigue	1	2	3	4	5	6	7
3. I am easily fatigued	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities	1	2	3	4	5	6	7
8. Fatigue is among my three most disabling symptoms	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life	1	2	3	4	5	6	7