Sleep Apnea and Psychological Functioning in Chronic Fatigue Syndrome

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ACKNOWLEDGEMENTS. This research was carried out at the Jewish General Hospital in Montreal, Quebec, Canada, with the assistance of a grant from the Canadian Institutes of Health Research (number MOP-77816).

COMPETING INTERESTS: None declared.

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Journal of Health Psychology

Los Angeles, London, New Delhi, Singapore and Washington DC
www.sagepublications.com
Vol 14(8) 1251–1267
DOI: 10.1177/1359105309344895

Abstract

Objectives were to explore: (1) whether sleep apnea/hypopnea syndrome (SAHS) should be considered a chronic fatigue syndrome (CFS) comorbidity, rather than a diagnostic exclusion criterion; and (2) to compare sleep/wake/psychopathology in individuals with CFS, controls and another illness. Participants (CFS, SAHS, controls) completed questionnaires and were evaluated for SAHS; 68 percent were subsequently diagnosed with SAHS. CFS participants with and without SAHS did not differ. Both clinical groups were less well adjusted than controls. We conclude that SAHS should not be an exclusion criterion for CFS and that psychological problems in CFS seem a consequence of coping with illness.

Keywords

- *chronic fatigue syndrome*
- *psychological adjustment*
- *sleep apnea*

THE TRADITIONALLY accepted definition of chronic fatigue syndrome (CFS) (Jason et al., 1999) as well as recent clarifications (e.g. Carruthers et al., 2003; Reyes et al., 2003) stipulate that the presence of a known primary sleep disorder, such as sleep apnea/hypopnea syndrome (SAHS), precludes the diagnosis of CFS. Presumably, this is because it is believed that a sleep disorder could account for the CFS symptoms. Yet, abnormalities of sleep in patients with CFS have been widely reported (Buchwald, Pascualy, Bombardier, & Kith, 1994; Fischler, 1999; Fossey et al., 2004; Le Bon et al., 2000; Morriss et al., 1993; Sharpley, Clements, Hawton, & Sharpe, 1997; Stores, Fry, & Crawford, 1998), and excluding individuals with primary sleep disorders from samples with classic CFS symptomatology has been inconsistently applied. Notably, individuals with CFS are not routinely sent for evaluation of sleep disorders. Therefore, it is likely that there is a high percentage of unrecognized sleep disorder in both CFS study participants and clinical patients.

As an example, in a previous study where the protocol required that participants be sent routinely to a sleep laboratory for polysomnographic (PSG) evaluation (Fossey et al., 2004), we were surprised to find that approximately 60 percent of our sample of individuals with CFS had a diagnosable primary sleep disorder such as sleep apnea/hypopnea syndrome (SAHS). What made these findings unexpected was that our sample consisted primarily of normal weight women in their late 30s and early 40s—a group not typically considered at risk for SAHS. Considering the extent of the physiologically based sleep-related problems, it is noteworthy that prior to participating in our study, neither the CFS patients nor their physicians had been aware that they had such a disorder. In that study, similar to a number of other reports in the literature (Carruthers et al., 2003; Gurbaxani, Goertzel, Jones, & Maloney, 2006; Krupp, Jandor, Coyle, & Mendelson, 1993; Reeves et al., 2006; Schaefer, 1995; Sharpley et al., 1997; Unger et al., 2004), we also found that almost all participants with CFS complained of nonrestorative sleep and/or difficulty initiating or maintaining sleep (89% and 86%, respectively; Fossey et al., 2004). Given such findings, the present investigation asks whether SAHS should continue to be considered an exclusion criterion for CFS, or whether SAHS and other sleep disorders should best be seen as frequent comorbidities of CFS.

Because CFS is a diagnosis of exclusion, with no clear tests or biological markers, many CFS patients have had the experience of being told that they are suffering from a disorder such as depression or somatization disorder (Fossey et al., 2004). Despite growing evidence that abnormal, objective biologic processes are present (Komaroff & Buchwald, 1998), many believe that CFS is primarily a psychological/psychiatric disorder because no physiological marker has been identified (e.g. Stewart, 1990). Patients with CFS have often been presented with the medical opinion that, 'It's all in your head'. Not only do they suffer from the symptoms of the illness, but they also often suffer from rejection and stigmatization by their family, friends and physicians (Bowen, Pheby, Charlett, & McNulty, 2005; Edwards, Thompson, & Blair, 2007; Ware, 1992). Although women without CFS typically suggest that the way to deal with fatigue is to, 'talk to others and get emotional support' (Karasz & McKinley, 2007), these alternatives are not readily available to many women with CFS, many of whom have long ago exhausted available help from friends, family and physicians alike.

In a previous study where we compared psychological adjustment and quality of life in individuals with CFS, narcolepsy and healthy controls we, too, found that psychological adjustment was poorer in the CFS than in the Healthy Comparison sample (Fossey et al., 2004). However, we also found that individuals with narcolepsy had poorer psychological adjustment than did healthy control participants. Moreover, we found no significant differences on any of the psychological adjustment variables evaluated between the two clinical groups: CFS and narcolepsy.

In Fossey et al.'s (2004) study, depression scores were within the normative range, although the scores of both clinical samples showed slightly elevated anxiety and somatization scores, as well as generally poorer psychological adjustment when compared to normative data. A similar pattern was noted when quality of life was evaluated, although participants with CFS reported the largest number of limitations of their functioning due to impaired health.

The pattern of elevated anxiety, but similar depression levels when compared with healthy control participants, has been documented in other CFS studies as well (e.g. Fischler, Cludydts, de Gucht, Kaufman, & de Meirleir, 1997). So too has the high degree of functional impairment that is comparable to that experienced in chronic medical

conditions, and that is even more severe than that experienced in clinical depression (e.g. Buchwald, Pearlman, Umali, Schmaling, & Katon, 1996). Depressed mood and elevated anxiety is also commonly seen in individuals suffering chronic pain (e.g. headache; Libman, 2008; McWilliams, Cox, & Enns, 2003). Because the role of psychological factors continues to be an issue, both in the CFS literature and in the lives of individuals with CFS (e.g. Ciccone, Weissman, & Natelson, 2008; Njoku, Jason, & Torres-Harding, 2007), the present study also explores psychological adjustment in individuals with CFS in addition to providing a profile of their sleep, quality of life and CFS symptoms.

The general goal for the present study was to contribute to improved diagnosis and treatment of CFS. To explore the question of whether primary sleep disorder, such as SAHS, should be seen as a comorbidity of CFS and not as a diagnostic exclusion criterion, we tested two hypotheses. If SAHS adds to or is responsible for symptoms of daytime fatigue and sleepiness, and therefore is an appropriate exclusion criterion for CFS, then it would be expected that: (1) as is the case for any individual with SAHS, participants who arrive with a CFS diagnosis and who are subsequently diagnosed with SAHS, should have worse scores on a variety of sleep and CFS-related daytime symptoms, such as fatigue and sleepiness, than those who are not diagnosed with SAHS (e.g. Patel, White, Malhotra, Stanchina, & Ayas, 2003); (2) as in the case of individuals with SAHS who are treated with continuous positive airway pressure (CPAP), participants with both CFS and SAHS who are treated with CPAP should improve on variables such as sleep quality and daytime fatigue and sleepiness compared to their untreated counterparts (e.g. Malhotra, Ayas, & Epstein, 2000).

We also set out to evaluate the assumption that individuals with CFS tend to have poor psychological adjustment by comparing the sleep/wake/psychological adjustment 'profile' of individuals with CFS with that of a Healthy Comparison group as well as that of another clinical sample: individuals who are sleepy and tired and have SAHS, but no CFS. To do this, we tested the hypothesis (3) that the sleep/wake/psychological adjustment profile of individuals with CFS would be worse than that of healthy individuals, but would not differ from that of individuals who suffer from another diagnosed sleep/fatigue related disorder (i.e. SAHS). Specifically, we expected that individuals who have CFS but no SAHS will not differ in psychological adjustment from individuals who have SAHS but no CFS, but that both clinical groups (i.e. CFS Only, and SAHS Only) would have worse scores on psychological adjustment than Healthy Comparison participants.

Method

Participants

Participants consisted of three groups: arrived with a diagnosis of CFS ($n = 66$; 59 females, seven males; mean age = 44.74, SD = 9.93), had a diagnosis of SAHS Only ($n = 22$; 19 females, three males; mean age = 53.59, SD = 4.64) and a convenience sample of 22 Healthy Comparison individuals with no diagnosed medical or psychiatric condition, no complaint of fatigue, sleepiness or insomnia and no diagnosable primary sleep disorder such as SAHS ($n = 22$; 17 females, five males; mean age = 41.86, SD = 8.90).

The CFS sample was recruited through physician referrals, CFS support groups and media advertisement. Our team neurologist confirmed the CFS diagnosis using Fukuda et al.'s (1994) diagnostic criteria, as well as standard medical evaluation and blood tests to rule out other medical disorders. Participants with SAHS were recruited, for a different arm of our research program, from the community through media publicity advertising a research study for older individuals suffering from 'daytime fatigue, sleepiness or insomnia'. A comprehensive evaluation was conducted first through interview and questionnaire by the research team and then through medical and overnight polysomnographic (PSG) assessment by our team respirologist. Those who were subsequently diagnosed with SAHS were selected for this study. Healthy Comparison group participants were recruited from the community and through personal contacts. Some of the participants went to the sleep laboratory for PSG ($n = 13$). In the case of participants recruited through personal contacts ($n = 9$), the cost and burdensome protocol of the laboratory PSG was not deemed warranted. Therefore, we used home sleep period recording to screen for apnea.

Characteristics of the three samples are presented in Table 1. The groups differed significantly on age, with the SAHS group being significantly older than both the CFS and the Healthy Comparison group,

Table 1. Sample characteristics for the CFS, SAHS only and Healthy Comparison groups

Sample	*CFS*	*SAHS only*	*Healthy Comparison*
N	66	22	22
Age (yrs):	44.74	53.59	41.86
Mean (SD)	(9.93)	(4.64)	(8.90)
Sex (*n*):	59 / 7	19 / 3	17 / 5
Female / Male			
Education (yrs):	15.49	17.25	14.45
Mean (SD)	(2.89)	(4.35)	(2.54)

Note: CFS = Chronic fatigue syndrome; SAHS = Sleep apnea-hypopnea syndrome

$F(2, 109) = 10.97$, $p < .001$. Participants had an average of 16 years of education with the SAHS group having an average of 2.8 more years of education than the comparison group, $F(2, 108) = 4.45$, $p < .05$. Chi-square tests failed to indicate a significant difference in the proportion of males to females in the three groups, $\chi^2 = 2.06$, $p = .357$.

Measures

Structured sleep history interview A modified version of the clinical instrument developed by Lacks (1987) was used to evaluate exclusion criteria, including the presence of medically based sleep disorders and major physical and psychiatric disorders. Most questions require a Yes/No answer, with prompts in case of suspected difficulty. This measure has been successfully used in our previous studies of sleep and aging (Fichten et al., 1995; Libman, Creti, Amsel, Brender, & Fichten, 1997a; Libman, Creti, Levy, Brender, & Fichten, 1997b).

Background information form (Libman, Creti, & Fichten, 1987; Libman et al., 1989) This measure provided information on age, sex and demographic variables.

Body Mass Index (BMI) The most common cause of obstructive sleep apnea in adults is obesity (Young et. al., 1993). The BMI is an index based on a person's height and weight that is a reliable indicator of body fat, and is used to screen weight categories that might be associated with health problems (e.g. Matsugawa et al., 1990), including obstructive sleep apnea. A BMI greater or equal to 30 kg/m^2 is considered to be obese.

Diagnosis of SAHS Participants in the two clinical groups and 13 of the Healthy Comparison group underwent polysomnography. They were monitored in a supervised sleep laboratory from 10.00pm to 7.00am. Monitoring included three leads EEG, EOG, bilateral anterior tibialis and chin EMG, ECG, pulse oximetry, nasal and oral airflow with thermistor and nasal pressure cannulae, microphone for snoring and respitrace bands for measurement of respiratory effort. Leg movements, apnea events and associated arousals were scored manually according to the scoring rules established by the Atlas Task Force of the American Sleep Disorders Association (1993) and the International Classification of Sleep Disorders-2 (American Academy of Sleep Medicine, 2005). Apnea disorder was defined as cessation of breathing lasting 10 or more seconds with a frequency of more than five times per hour. Participants were diagnosed with hypopnea when there was 50 percent or more decrease in airflow regardless of oxygen desaturation, a 30 percent or more decrease in airflow with 3 percent or more oxygen desaturation or 30 percent or more decrease in airflow with a subsequent cortical arousal.

The home sleep period assessment was performed with a SnoreSat Recorder (SegaTech Electronics Inc., Calgary, Canada). This device has been compared to overnight polysomnography and found to provide a close estimate of the Apnea/Hypopnea Index (AHI) ($r = .97$) as well as excellent diagnostic sensitivity (98%) and specificity (88%) for obstructive sleep apnea (OSA) in a sample of patients with suspected OSA (Vazquez et al., 2000). Briefly, participants were instructed in the afternoon about the use of the device and returned home with written instructions. They slept at home on a night without any unusual upper respiratory tract symptoms such as acute nasal congestion, and recorded the time from when they turned off the lights to go to sleep to the time they awoke in the morning. This device records pulse oximetry, nasal airflow with nasal pressure cannulae, microphone for snoring and respitrace bands for measurement of respiratory effort. Records underwent automated scoring which was validated by visual inspection of the raw data disclosed in 10-minute epochs. Respiratory disturbance indices were adjusted for any time spent with invalid recording or persistent movement suggesting wakefulness.

Sleep Questionnaire (Libman, Fichten, Bailes, & Amsel, 2000) This brief questionnaire, which provides retrospective information that is often obtained from a sleep diary, was used to assess participants' usual sleep experiences during the past

typical month, including hours slept per night, duration and frequency of nocturnal arousals, bedtimes and arising times, frequency (0–7 days per week) of difficulty falling asleep or getting back to sleep after nocturnal awakenings and frequency of naps. The information provided allowed us to: (1) establish the presence of a sleep complaint (i.e. Do you have insomnia? Yes/No); (2) specify the duration of the insomnia problem; (3) diagnose the presence or absence of difficulty initiating or maintaining sleep in accordance with typically used research criteria (i.e. at least 31 minutes of undesired awake time at least three times per week, problem duration at least six months—Lichstein, Durrence, Taylor, Bush, & Riedel, 2003); (4) obtain self-report estimates of sleep parameters and the number of days per week of non-refreshing sleep; (5) compute sleep efficiency (percent of bedtime spent asleep); and (6) obtain ratings of respondents' subjective perceptions of their sleep quality and their daytime functioning on 10-point Likert-type scales. Data indicate good test–retest reliability: *r* values range from .58 to .92 for intervals ranging from two weeks to 15 months (Fichten et al., 1995). High correlations between equivalent scores on this measure and on a daily sleep diary were also found (e.g. *r* = .83, .64 and .69 for total sleep time (TST), sleep onset latency (SOL) and waking after sleep onset (WASO), respectively; Libman et al., 2000).

Actigraphy The Actitrac (IM Systems Co., Baltimore, MD, United States), an actigraphy monitor resembling a wristwatch, was used to examine daytime rest and activity during a seven-day period. Activity was recorded every second from the non-dominant wrist. The average activity level, measured as acceleration units of milliG (mG: Earth's gravitational acceleration), was used as the main dependent variable. Other variables include average duration of active and inactive periods. Data were processed and scored with the IM Systems software and algorithm (version 8).

Empirical Sleepiness and Fatigue Scales Since existing scales measuring fatigue and sleepiness confounded the two concepts, the Empirical Sleepiness and Fatigue Scales were developed by Bailes et al. (2006) through correlation and factor analysis of all items from four popular measures purporting to measure sleepiness and fatigue: Stanford Sleepiness Scale (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973), Epworth Sleepiness Scale (Johns, 1991), Fatigue Severity Scale (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989) and the Chalder Fatigue Scale (Chalder et al., 1993). The Empirical Sleepiness Scale consists of six items from the Epworth Sleepiness Scale while the Empirical Fatigue Scale consists of one item from the Fatigue Severity Scale and two from the Chalder Fatigue Scale. The two Empirical Scales represent different constructs that were found to have distinctive patterns of associations and were only minimally correlated with each other in three different samples (*r* = .06 to .33). Sleepiness can be generally defined as sleep propensity and fatigue as diminished energy. Analyses reported by the Scales' authors indicate good test–retest reliability over two different four-hour periods for both the Sleepiness (*r* = .69, and .88) and the Fatigue (*r* = .87, and .91) Empirical Scale. Internal consistency was also good, with Cronbach's alpha scores for the Empirical Sleepiness Scale ranging from .92 to .95 and those for the Empirical Fatigue Scale ranging from .74 to .86. Extensive validity information is provided by the authors of the Scales for two samples; this shows that the two measures are logically related to a large number of criterion variables. Higher scores indicate greater sleepiness or fatigue.

Beck Depression Inventory (BDI-II): Primary Care Subscale (PC) The seven-item PC subscale of the BDI-II (Beck, Steer, & Brown, 1996) was used in this study to evaluate the affective and cognitive symptoms of depression independent of fatigue, sleepiness, insomnia and agitation. Beck et al. report that the test–retest reliability for the PC subscale is .82, while its internal consistency is .86. Items are scored on a four-point scale (0–3). Scores are summed and produce a range from 0 to 21. Higher scores indicate greater depression.

Spielberger State-Trait Anxiety Inventory—Form Y2 (STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) This frequently used measure consists of two separate 20-item self-report scales for measuring trait and state anxiety. In the present investigation only trait anxiety was evaluated. The trait measure asks people to describe how they generally feel on four-point Likert-type scales (1 = almost never, 4 = almost always). Scores range from 20 to 80. The authors report a mean of 35 (SD = 9) for a normative sample of adults. Higher scores indicate greater anxiety. Psychometric properties of this scale have been shown to be excellent with test–retest reliability data, based on student samples, ranging from .65 to .86,

and internal consistency indicating a median alpha coefficient of .91 for a working adult sample.

Brief Symptom Inventory (BSI) (Derogatis, Rickels, & Rock, 1976) The Global Severity Index (GSI) of this 53-item self-report psychological symptom inventory was used as a global measure of psychopathology. This score has a possible range of 0 to 4. The measure's authors report a mean of .30 (SD = .31) for a normative sample of adults. The BSI is a brief version of the SCL-90 (Derogatis, 1977)—a frequently used instrument with acceptable reliability and validity. Validation data indicate correlations from .92 to .98 between the symptom dimensions and global indices of the BSI and the SCL-90. Lower scores indicate better adjustment.

SF-36 Health Survey (Ware, Snow, Kosinski, & Gandek, 2000) This popular 36-item measure was used to assess quality of life in eight health domains: (1) limitations in physical activities because of health problems; (2) limitations in social activities because of physical or emotional problems; (3) limitations in usual role activities because of physical health problems; (4) bodily pain; (5) general mental health (psychological distress and well-being); (6) limitations in usual role activities because of emotional problems; (7) vitality (energy and fatigue); and (8) general health perceptions. Ware et al. (2000) report reliability data based on both patient and non-patient samples. Reliability of the subscales ranged from .64 to .96. The SF-36 has demonstrable validity in that the subscales were found to correlate with ability to work, utilization of health services, as well as other mental health and quality of life measures. Low scores on all subscales indicate disability due to illness; high scores indicate better functioning due to relatively good health.

Satisfaction with Life Scale Developed by Diener, Emmons, Larsen, and Griffen (1985), this scale evaluates positive rather than negative aspects of subjective well-being. It consists of five items which use a seven-point Likert scale. Higher scores indicate greater life satisfaction. Data reported by the authors as well as in later investigations (Pavot, Diener, Colvin, & Sandvik, 1991) indicate good psychometric properties; the measure has been shown to be internally consistent (item-total correlations varied from .55 to .80), items loaded on a single factor, and scores were found to be highly correlated with other measures of life satisfaction. What makes this measure different from most of the others used in the present investigation is that it measures the presence of good quality of life, rather than the absence of problems.

Procedure

The research ethics committees of both the SMBD-Jewish General Hospital and the Mount Sinai Hospital of Montreal approved the research protocol. All participants were volunteers and gave their informed consent. They were screened with the Structured Sleep History Interview for comorbid diagnoses and excluded if: (1) they suffered from a current major psychiatric illness; (2) had another known medical condition related to fatigue, sleepiness, arthralgia or insomnia (other than fibromyalgia, which was not excluded from the CFS sample); and (3) they were working rotating/split shifts or recently traveled across time zones. Inclusion criteria included being a community resident and having sufficient cognitive and language skills to complete the measures in English or French.

Following the initial screening, all participants responded to a lengthy questionnaire battery assessing aspects of their nocturnal and daytime functioning. The CFS and Healthy Comparison samples then wore the Actitrac actigraphy watch that recorded both daytime and nocturnal activity levels for seven days. The participants with SAHS did not wear the Actitract as it was not a requirement of that arm of the research program.

Subsequently, our sleep specialist team member conducted a general medical and sleep disorders assessment. Participants then underwent a single night of overnight polysomnography (PSG) in a sleep laboratory. This took place anywhere from one week to six months after the interview/evaluation session and was dependent on sleep laboratory and participant availability. Healthy Comparison participants were evaluated in their home with the SnoreSat Recorder.

On the basis of PSG and/or SnoreSat findings diagnosis of sleep apnea/hypopnea syndrome was carried out by a certified respirologist in accordance with the International Classification of Sleep Disorders—2 (American Academy of Sleep Medicine, 2005) and American Sleep Disorder Association (1999) and American Sleep Disorders Association, Diagnostic Classification Steering Committee (2005). All CFS participants who were diagnosed with SAHS were offered a three-month

treatment with CPAP at no cost. Those who agreed returned for an additional night in the sleep lab to determine the appropriate CPAP airflow pressure needed to reduce SAHS. Participants were given three months to adjust to using the CPAP and make any changes necessary to the breathing apparatus. Subsequently, participants completed the same battery of questionnaires as in the assessment phase. The CFS plus SAHS participants were classified as: Compliant if they reported use of the CPAP intervention 'on a regular basis' at post-testing and Noncompliant if they reported not having started or having stopped using the CPAP intervention before post-testing. The remaining CFS Plus SAHS participants either refused CPAP treatment or failed to return for a post-CPAP assessment.

At the end of the investigation, participants were given detailed feedback about their results of the study. If any sleep disturbances were detected, appropriate referrals were made for further assessment and/or treatment.

Analyses

Chi-square tests were applied to assess differences in the proportion of males and females in the SAHS and CFS groups. Analysis of variance (ANOVA) was used to test hypotheses related to group differences. When age and BMI differences were significant, they were treated using analysis of covariance (ANACOVA). Bonferroni corrections were applied to correct for the numerous comparisons tested. Paired *t*-tests were used to compare pre- to post-testing difference scores for CFS Plus SAHS Compliant and Noncompliant participants.

Results

How do individuals who have CFS with and without sleep apnea/hypopnea syndrome (SAHS) compare? Testing Hypothesis 1

Among the 66 participants with CFS, we found 45 who also had SAHS (CFS Plus SAHS) and 21 who had not been diagnosed with SAHS (CFS Only). To evaluate the role of SAHS in CFS we first compared the scores of these two groups. The proportion of female to male participants was 38:7 in the CFS Plus SAHS group and 21:0 in the CFS Only group, $\chi^2 = 3.65$, $p = .056$. With respect to severity of SAHS, as expected, the Respiratory Disturbance Index (RDI), as measured by PSG, was significantly higher in the group of CFS participants diagnosed with SAHS than in the CFS Only group, $F(1, 63) = 26.52$, $p < .001$. Body Mass Index (BMI) indicated that participants with CFS Plus SAHS ($M = 26.35$, SD = 6.47) were significantly heavier than CFS Only participants ($M = 22.34$, SD = 4.46), $F(1, 59) = 6.20$, $p < .05$ (see Table 2).

When PSG scores of participants with CFS Plus SAHS were compared with those of the SAHS Only group, no significant difference was found on either the Respiratory Disturbance Index (RDI), $F(1, 65) = 1.73$, $p = .192$ or the BMI, $F(1, 61) = 3.90$, $p = .053$, even when age was covaried.

Because there was a significant BMI difference between the two groups, ANACOVAs, with BMI as a covariate, were performed to compare scores of CFS Plus SAHS and CFS Only participants on the 27 scores assessing variables important to the experience and symptoms of CFS as well as SAHS: sleep variables, daytime fatigue and sleepiness, other aspects of CFS symptomatology, psychological adjustment, quality of life and objective daytime activity (actigraphy) measures (see Table 2). Given the number of comparisons, a Bonferroni correction was applied; therefore only a p value < .002 was considered significant. Only four of the 27 comparisons were significant before the Bonferroni correction to the alpha level. Afterwards, none were found to be significant.

What happens to CFS patients with SAHS after they are treated? Testing Hypothesis 2

CPAP treatment was offered to all CFS Plus SAHS participants. If SAHS contributes substantially to CFS-related symptomatology, then one would expect that treating the SAHS should make perceptible changes in CFS-related symptoms such as daytime fatigue and sleepiness.

To evaluate this hypothesis we compared scores of CFS Plus SAHS participants who were Compliant with CPAP treatment ($n = 10$) with those of CFS Plus SAHS patients who were Noncompliant with CPAP treatment ($n = 7$). Change pre- to three months post-CPAP treatment was examined for participants who completed measures at these two testing times.

Because of the small sample sizes we reduced the number of dependent variables by selecting variables traditionally perceived as pertinent to CFS and SAHS. These included: daytime variables

Table 2. Means for CFS participants with and without SAHS on a variety of variables

Variables	*CFS Plus SAHS*	*CFS Only*	*d.f.*	*F*	*Sig.*
Sample Characteristics					
N	45	21			
Sex (female / male) (Chi Square)	38 / 7	21 / 0	1	(3.65)	0.0560
Age(yrs): Mean (SD)	45.96 (10.10)	42.14 (9.25)	1.65	2.15	0.1480
Education (yrs): Mean (SD)	15.61 (3.10)	15.42 (2.43)	1.64	0.24	0.6270
BMI (Body Mass Index)	26.35 (6.47)	22.34 (4.46)	1,59	6.20	0.0160
RDI[1] (Respiratory Disturbance Index)	19.42 (12.73)	4.61 (2.22)	1,63	26.52	0.0000
Sleep Variables					
Sleep Quality[2]	3.12 (1.49)	4.50 (2.24)	1,51	6.23	0.0160
Sleepiness Scale[1]	8.03 (4.24)	7.18 (4,68)	1,51	0.03	0.8640
Napping Frequency (days/wk)	4.53 (2.35)	4.53 (2.54)	1,51	0.16	0.6950
Sleep Efficiency	0.77 (0.17)	0.77 (0.20)	1,51	0.05	0.8210
TST (Total Sleep Time) (hrs)	7.04 (1.82)	7.68 (1.85)	1,53	1.40	0.2420
SOL (Sleep Onset Latency) (hrs)	0.82 (0.59)	1.29 (0.94)	1.62	5.44	0.0229
WASO (Wake After Sleep Onset) (hrs)	1.28 (0.82)	0.69 (0.67)	1.48	5.37	0.0250
Morning Headaches (days/wk)	2.02 (2.54)	3.06 (2.95)	1.49	2.51	0.1200
CFS Symptoms					
Fatigue Scale[1]	14.62 (2.73)	15.80 (2.67)	1,51	1.15	0.2890
Non-refreshing Sleep[1]	2.37 (1.82)	2.60 (2.21)	1,51	0.00	0.9980
Concentration[1]	6.74 (2.44)	7.2 (2.55)	1,51	0.42	0.5190
SF36 Body Pain[2]	39.94 (26.64)	38.05 (23.36)	1,50	0.43	0.5140
Daytime Headaches (days/week)	1.74 (1.32)	1.70 (1.34)	1,38	0.00	0.9890
Psychological Variables[1]					
STAI Total Anxiety Score	45.88 (8.04)	43.61 (9.47)	1.49	0.45	0.5070
Depression—BDI (PCI Sub-total)	4.91 (3.84)	5.83 (3.45)	1.49	1.30	0.2590
BSI (Global Severity Index)	1.13 (0.77)	1.28 (0.62)	1.48	0.65	0.4250
Quality of Life[2]					
SF36—Physical Functioning	45.29 (22.29)	48.68 (21.78)	1,50	0.04	0.8520
SF36—Role Physical	2.94 (17.15)	3.95 (12.54)	1,50	1.70	0.1980
SF36—General Health	33.15 (15.40)	38.74 (13.91)	1,50	1.04	0.3120
SF36—Vitality	22.94 (12.98)	22.89 (15.84)	1,50	0.02	0.8870
SF36—Social Functioning	35.29 (17.54)	39.47 (19.21)	1,50	0.99	0.3240
SF36—Role; Emotional	50.00 (47.32)	52.63 (42.04)	1,50	0.02	0.8990
SF36—Mental Health	54.94 (17.73)	60.21 (17.31)	1,50	1.47	0.2320
Life Satisfaction	16.66 (6.85)	17.50 (8.30)	1,36	0.02	0.8870
Actigraphy					
Average Activity Level	10722.92 (12228.38)	8043.49 (6812.26)	1,33	0.29	0.5960
Average Duration of Active Periods	133.73 (113.76)	113.95 (66.77)	1,30	0.20	0.6590
Average Duration of Inactive Periods	7.92 (5.00)	6.02 (2.37)	1,30	1.95	0.1730

Notes: Sample sizes vary due to missing data for some variables. The boxed comparison is significant after a Bonferroni correction to the alpha level.

[1] Lower scores indicate better functioning.

[2] Higher scores indicate better functioning.

CFS = Chronic fatigue syndrome, SAHS = Sleep apnea-hypopnea syndrome, STAI = State-Trait Anxiety Inventory, BDI = Beck Depression Inventory, BSI = Brief Symptom Inventory.

(fatigue and sleepiness); a quantitative and a qualitative sleep measure (sleep efficiency and sleep quality); non-refreshing sleep; and a 'quality a life' variable (General Health subscale of the SF-36, Ware et al., 2000). Pre- to post-testing difference scores were compared using paired *t*-tests (CFS Plus SAHS Compliant vs CFS Plus SAHS Noncompliant). Table 3 shows the means pre- and post-CPAP intervention. No significant differences were found between the two groups on any of the six measures. The test results and examination of the pre- and post-means indicates that the CPAP

Table 3. Means and text results for CPAP Noncompliant and CPAP Compliant groups

		Pre-Testing		*Post-Testing*		*Paired t-tests of difference scores*		
Variables	*N*	*Mean*	*Std. Deviation*	*Mean*	*Std. Deviation*	*d.f.*	*F*	*Sig.*
Sleep Quality[1]								
Noncompliant	7	2.86	1.57	3.43	2.30	1,15	3.69	0.074
Compliant	10	3.00	1.41	5.70	2.58			
Non-refreshing Sleep[1]								
Noncompliant	7	2.43	2.15	2.86	3.08	1,15	3.47	0.082
Compliant	10	1.65	1.20	4.55	2.97			
Sleep Efficiency[2]								
Noncompliant	7	0.81	0.16	0.79	0.21	1,15	0.21	0.653
Compliant	10	0.83	0.20	0.84	0.16			
Fatigue[2]								
Noncompliant	7	15.86	2.91	16.71	2.21	1,15	0.25	0.629
Compliant	10	13.70	1.70	13.80	3.16			
Sleepiness[2]								
Noncompliant	7	11.14	3.98	9.29	4.50	1,15	0.40	0.538
Compliant	10	9.20	2.97	6.00	4.32			
General Health Subscale[1]								
Noncompliant	6	37.67	18.16	38.17	20.46	1,14	0.26	0.617
Compliant	10	30.90	13.64	35.10	23.04			

Notes: Sample sizes vary due to missing data for some variables.
[1] Lower scores indicate worse functioning.
[2] Lower scores indicate better functioning.

treatment did not result in any substantial changes in CFS-related symptomatology.

Sleep/wake/psychological adjustment 'profile' of individuals with CFS: testing Hypothesis 3

Hypothesis 3 states that individuals with CFS will have worse scores on a variety of psychological adjustment measures than Healthy Comparison group individuals, but that their scores would not differ from those of individuals with another sleep/fatigue diagnosis. We tested this hypothesis by comparing the scores of three groups of participants: (a) CFS Only; (b) SAHS Only; and (c) Healthy Comparison. Table 4 presents the means and standard deviations of the three psychological variables evaluated: anxiety (Spielberger State-Trait Anxiety Inventory (STAI) trait score, Spielberger et al., 1983), depression (Beck Depression Inventory (BDI-II): Primary Care Subscale (PC), Beck et al., 1996) and general psychopathology (GSI score of the Brief Symptom Inventory (BSI), Derogatis, 1977). Because there was a significant age difference among the three groups, ANCOVA comparisons, with age as a covariate, were performed.

Means and test results in Table 4 show that all three comparisons were highly significant. Post-hoc Tukey HSD tests show that both clinical groups had significantly worse scores than the Healthy Comparison group on all three measures. The CFS Only group had significantly higher general psychopathology (BSI) scores than the SAHS Only group, although there was no significant difference between the two clinical groups on either anxiety or depression. In order to further clarify the clinical relevance of these findings, effect sizes were calculated. Generally, the effect sizes were large for the comparisons between each of the clinical groups and the Healthy Comparison group. The single significant difference between the two clinical groups had a moderate effect size.

To provide a profile of individuals with CFS on a range of sleep, wake, activity and quality of life variables, we compared the scores of the three groups (CFS Only, SAHS Only and Healthy Comparison) on variables evaluating sleep, fatigue and sleepiness,

Table 4. Means and test results for CFS Only, SAHS Only and Healthy Comparison groups on psychological variables

Variables[1] *group*	*Mean*	*SD*	*N*	*d.f.*	*F*	*Sig. p =*	*Post-hoc test*	*Cohen's d*	*Effect size*
Anxiety (STAI)									
CFS Only	43.84	9.26	19	2,59	6.73	0.0023	CFS>H**	1.12	large
SAHS Only	41.11	10.68	22				SAHS>H*	0.79	large
Healthy Controls	32.82	10.35	22						
Depression (BDI)									
CFS Only	5.58	3.53	19	2,59	7.32	0.0015	CFS>H***	1.4	large
SAHS Only	3.41	4.32	22				SA>H*	0.56	
moderate									
Healthy Controls	1.50	2.13	22						
Psychopathology (BSI)									
CFS Only	1.26	0.61	18	2,57	17.25	0.0000	CFS>H***	2.03	large
SAHS Only	0.83	0.62	21				A>H**	1.09	large
Healthy Controls	0.31	0.26	22				CFS>A*	0.7	moderate

other CFS symptoms, quality of life and activity level (actigraphy). Means, standard deviations and test results may be seen in Table 5. Given the large number of comparisons, a Bonferroni correction was applied to the alpha level; therefore only a p value < .002 is considered significant.

Sleep variables Of seven sleep variables examined (see Table 5), significant differences were found on two: scores for the Healthy Comparison group were significantly higher on Sleep Quality and lower on Nap Frequency than those of both clinical groups. The two clinical groups differed significantly from each other on Nap Frequency, with the SAHS Only group scoring lower than the CFS Only group.

CFS symptoms We selected for comparative evaluation the following five CFS-associated symptoms: Fatigue; Feeling Refreshed in the Morning; Ability to Concentrate; Body Pain; and Daytime Headaches (Table 5). The ANCOVA revealed significant differences among groups. Post-hoc tests indicate that the three groups, CFS Only, SAHS Only, Healthy Comparison, differed significantly from each other on three variables: Fatigue; Concentration; and Pain. Means indicate that the Healthy Comparison group consistently had the best scores, while the CFS group had the worst scores on these variables. The Healthy Comparison group had significantly higher scores on Feeling Refreshed in the Morning and significantly lower scores on Daytime Headaches than the CFS Only group; the two clinical groups did not differ significantly from each other.

As can be seen in Table 5 participants in the SAHS Only group were heavier than participants with CFS Only. As would be expected, SAHS Only participants manifested a significantly higher Respiratory Disturbance Index (RDI) score compared to CFS Only individuals.

Quality of life variables These include the seven remaining scales of the SF-36 (Body Pain was discussed with the CFS symptoms) and the Satisfaction with Life Scale (Diener et al., 1985). Results indicate that the three groups differed significantly from each other on four SF-36 scales. Means in Table 5 indicate that the Healthy Comparison group had the best functioning scores while the CFS Only group had the worst. Healthy Comparison participants' scores were higher than those of CFS Only participants on the Satisfaction with Life Scale.

Actigraphy variables Although one of the three variables showed significant differences between the CFS Only and the Healthy Comparison group in the direction of the latter being more active, this difference was not maintained when Bonferroni corrections were applied (see Table 5).

Discussion

SAHS as a comorbidity of CFS, not as a diagnostic exclusion criterion (Goal 1: Hypotheses 1 and 2)

Two sets of analyses examined whether sleep apnea/hypopnea syndrome (SAHS) should be considered

Table 5. Means and Test Results for CFS Only, SAHS Only, and Healthy Comparison Groups on a Variety of Variables

	CFS Only Group N = 21		*SAHS Only Group N = 22*		*Healthy Comparison Group N = 22*		*Significance Tests*					
Variables	*Mean*	*Std. Deviation*	*Mean*	*Std. Deviation*	*Mean*	*Std. Deviation*	*d.f.*	*F*	*Sig. p =*	*Post-Hoc Test*		
BMI (Body Mass Index)	22.64	(4.46)	30.07	(8.23)	23.98	(5.37)	2,50	5.86	0.0020			
RDI (Respiratory Deisturbance Index)	4.61	(2.22)	24.69	(19.83)	5.31	(5.00)	2,58	12.37	0.0000		SAHS>H**	CFS<SAHS***
Sleep Variables												
Sleep Quality[2]	4.52	(2.18)	4.55	(2.40)	7.98	(1.56)	2,61	16.46	0.0000	CFS<H***	SAHS<H***	
Sleepiness Scale[1]	7.12	(4.57)	7.52	(4.45)	3.95	(2.85)	2,60	4.05	0.0224			
Naps-days/wk	4.64	(2.53)	2.55	(2.26)	1.05	(1.68)	2,61	15.51	0.0000	CFS>H***	SAHS>H***	CFS>SAHS**
Sleep Efficiency	0.77	(0.19)	0.81	(0.19)	0.86	(0.29)	2,61	2.24	0.1147			
TST (Total Sleep Time) (hrs)	7.67	(1.81)	6.94	(1.76)	7.36	(1.17)	2,61	0.58	0.5635			
SOL (Sleep Onset Latency) (hrs)	1.25	(0.93)	0.77	(1.10)	0.29	(0.19)	2,59	6.42	0.0030			
WASO (Wake After Sleep Onset) (hrs)	0.73	(0.67)	1.05	(1.43)	0.50	(0.88)	2,59	0.26	0.7737			
Morning Headaches (days/week)												
CFS Symptoms												
Fatigue Scale[1]	15.86	(2.61)	11.55	(4.01)	7.18	(4.14)	2,61	33.39	0.0000	CFS>H***	SAHS>H*	CFS>SAHS*
Non-refreshing Sleep[1]	2.62	(2.16)	3.91	(1.82)	5.82	(3.14)	2,61	9.14	0.0003	CFS<H***		
Concentration[1]	7.14	(2.50)	4.64	(2.30)	2.32	(1.62)	2,61	26.99	0.0000	CFS>H***	SAHS>H*	CFS>SAHS***
SF36 Body Pain[2]	37.75	(22.78)	59.05	(26.74)	79.14	(24.69)	2,60	14.33	0.0000	CFS<H***	SAHS<H*	CFS<SAHS*
Daytime Headaches (days/week)	1.73	(1.27)	na	na	0.62	(0.65)	1,21	7.65	0.0116			
Quality of Life[2]												
SF36—Physical Functioning	47.75	(21.61)	66.14	(22.20)	87.73	(21.42)	2,60	18.01	0.0000	CFS<H***	SAHS<H**	
SF36—Role Physical	3.75	(12.23)	39.77	(43.41)	86.36	(31.55)	2,60	34.01	0.0000	CFS<H***	SAHS<H***	CFS<SAHS**
SF36—General Health	38.90	(13.56)	56.45	(20.93)	83.18	(13.69)	2,60	38.47	0.0000	CFS<H***	SAHS<H***	CFS<SAHS*
SF36—Vitality	23.50	(15.65)	38.18	(20.44)	61.82	(21.96)	2,60	19.81	0.0000	CFS<H***	SAHS<H**	CFS<SAHS*
SF36—Social Functioning	38.75	(18.98)	63.07	(27.68)	88.07	(15.66)	2,60	27.24	0.0000	CFS<H***	SAHS<H**	CFS<SAHS**
SF36—Role; Emotional	51.67	(41.15)	63.64	(45.90)	83.33	(32.12)	2,60	3.27	0.0450			
SF36—Metal Health	61.20	(17.42)	68.91	(18.76)	75.27	(20.64)	2,60	2.93	0.0612			
Life Satisfaction	17.64	(7.89)	na	na	29.83	(4.06)	1,20	21.48	0.0002			
Actigraphy												
Average Activity Level	8043.49	(6,812.26)	na	na	14872.33	(8,316.57)	1,19	3.70	0.0695			

(Continued)

Table 5. (Continued)

Variables	*CFS Only Group N = 21*		*SAHS Only Group N = 22*		*Healthy Comparison Group N = 22*		*Significance Tests*			
	Mean	*Std. Deviation*	*Mean*	*Std. Deviation*	*Mean*	*Std. Deviation*	*d.f.*	*F*	*Sig. p =*	*Post-Hoc Test*
Average Duration of Active Periods	113.95	(66.77)	na	na	259.68	(114.98)	1,19	11.91	0.0027	
Average Duration of Inactive Periods	6.02	(2.37)	na	na	7.51	(7.60)	1,19	0.93	0.3476	

Notes: Sample sizes vary due to missing data for some variables. Boxed items significant after a Bonferroni adjustment to the alpha level.
* $p < .05$, ** $p < .01$, *** $p < .001$.
[1] Lower scores indicate better functioning.
[2] Higher scores indicate better functioning.
CFS = Chronic fatigue syndrome, SAHS = Sleep apnea-hypopnea syndrome, H = Healthy Comparison, STAI = State-Trait Anxiety Inventory, BDI = Beck Depression Inventory, BSI = Brief Symptom Inventory.

a comorbidity or an exclusionary criterion in the diagnosis of CFS. To test Hypothesis 1, which stated that if SAHS is to be considered an exclusionary criterion, then individuals with a CFS diagnosis who are subsequently diagnosed with SAHS should have worse scores on a variety of sleep and daytime symptoms such as fatigue and sleepiness than those individuals with CFS who are not diagnosed with SAHS, we compared the scores of participants with CFS who were subsequently diagnosed with SAHS with those of participants with CFS who had no SAHS. There was no support for this hypothesis as we found no significant differences on a wide range of sleep, fatigue, sleepiness, other CFS-related symptoms, psychological adjustment, quality of life and actigraphy-based activity measures. When conducting 27 ANOVAs, with an alpha level of .05, one would expect two significant values by chance alone: we found only one. Although there is no means of proving the null hypothesis, these findings do suggest that individuals with CFS, with and without SAHS, do not differ from each other in important ways. CFS symptomatology is equally prominent in both groups.

A second set of analyses tested Hypothesis 2, which stated that participants with both CFS and SAHS who are treated with CPAP should improve on variables such as sleep quality and daytime fatigue and sleepiness compared to their untreated counterparts. We did this by comparing the scores of two small samples of individuals with CFS: those who were subsequently diagnosed with SAHS and were compliant with the CPAP treatment and those with CFS Plus SAHS who were noncompliant with CPAP. If SAHS should be considered an exclusionary factor, then one would have expected participants compliant with the treatment to have a greater improvement on CFS-related symptoms than those who were noncompliant. We did not find this to be the case. Thus, the treatment of SAHS appears to be irrelevant to the presentation of CFS and its most prominent feature of daytime fatigue.

The etiology and pathophysiology of CFS has not been established; the disorder has been conceptualized on a spectrum of stress-related, functional disorders. One prominent current theory is that neuroendocrine components of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous systems have been deregulated (Holtorf, 2007; Shaver, 2003). It has been proposed previously that such deregulation is associated with sleep fragmentation. The deregulation of the neurophysiological

stress response, together with associated sleep fragmentation, has been hypothesized to play a causal role in sleep disordered breathing such as sleep apnea/hypopnea syndrome in other stress-related conditions as well (Krakow et al., 2002). In the context of such a conceptualization, the pattern of our findings supports the interpretation that the high incidence of sleep apnea/hypopnea syndrome in CFS is likely a correlate or consequence of the illness, rather than a competing diagnosis.

In summary, our present findings, as well as related aspects of the literature, support our position that SAHS should be considered a comorbidity, and not an exclusionary factor, in the diagnosis of CFS.

Comparative sleep/wake and psychological adjustment 'profile' of individuals with CFS (Goal 2: Hypothesis 3)

We tested the prevailing notion (Hypothesis 3) that individuals with CFS, defined in the traditional way (i.e. only those who do not have SAHS), will have worse scores on a variety of psychological adjustment measures than healthy individuals. But we added the caveat that their scores would not differ from those of individuals with another clinical disorder in which daytime fatigue is a prominent component. To evaluate this possibility we selected as a comparison sample individuals who did not have CFS but who did have a diagnosed, but as yet untreated, SAHS.

Our results show that individuals with CFS did, indeed, experience worse psychological adjustment than Healthy Comparison participants. But so did SAHS patients. Moreover, the two clinical groups (CFS Only, SAHS Only) were not significantly different from each other on two of the three measures of psychological adjustment: anxiety and depression, although the CFS group did experience worse adjustment than the SAHS Only group on global mental health, as measured by the BSI (Derogatis et al., 1976).

We also compared quality of life, sleep, CFS symptoms and activity levels of the three groups (CFS Only, SAHS Only, Healthy Comparison). Overall, the results show better functioning in the Healthy Comparison group than in the two clinical groups, who generally did not differ from each other. When there were differences, the CFS group had the worst scores. In particular, individuals with CFS had the worst scores on daytime fatigue, although daytime sleepiness, as well as sleep quality and quantity were similarly impaired for participants in both clinical groups.

Examination of the quality of life scores of the three samples partially explains the psychological findings, as the scores of the CFS sample were often less than half that of the scores of the Healthy Comparison group. This suggests that quality of life is very seriously impaired in individuals with CFS (Goudsmit, Stouten, & Howes, 2009; Libman, 2008). It is notable that our findings reflect a dramatic impairment in quality of life for people with CFS, even though participants with comorbid clinical depression (they were screened out in our sample) and those with profound physical limitations (incapable of following the rigorous study protocol) are not represented in our study.

Limitations

Several limitations of the current investigation should be noted. The most important of these is the small sample sizes involved in several analyses, which may put the generalizability of the findings into question. Because it is known that there is a higher rate of sleep disorder in older individuals, another concern is the age difference in the two clinical samples. Although we covaried age in the analyses, this may not have been a sufficient control. The healthy comparison sample was recruited in a different manner from the two clinical samples and a few members of the healthy sample were not tested for the possible presence of sleep apnea/hypopnea syndrome in the sleep laboratory using PSG. Instead, we were able to test for the absence of SAHS by using the portable SnoreSat device. Although the SnoreSat has acceptable reliability and validity, the gold standard in the diagnosis of sleep apnea/hypopnea syndrome is PSG. Finally, we tested the effects of CPAP after only three months of use. A longer period of CPAP use may have resulted in more benefits (e.g. Malhotra et al., 2000).

Summary and conclusions

Our data suggest that sleep apnea/hypopnea syndrome should be considered a comorbidity rather than an exclusionary criterion for the diagnosis of CFS. Treating our participants with CFS who also had sleep apnea/hypopnea syndrome with continuous positive airway pressure (CPAP) did not appear to improve their functioning profile. Nevertheless, apnea treatment for these individuals is still recommended. Treatment of sleep apnea has traditionally been aimed at reducing the number of episodes of apnea and hypopnea, the number of arousals and oxyhemoglobin desaturation during sleep. Recently

it has been found that long-term CPAP treatment reduces nocturnal cardiac ischemic episodes and improves daytime blood pressure level and left ventricular function (Lattimore, Celermajer, & Wilcox, 2003). In the literature, these reductions have been correlated with a decrease in subjective daytime fatigue and sleepiness (e.g. Guilleminault, 1994) and objective rate of motor-vehicle accidents (Bridges et al., 2003). We were not able to demonstrate reduced daytime sleepiness or fatigue in the present study, possibly because of the short treatment time interval used (three months), because of the small sample or, possibly, because these variables are not susceptible to sufficient improvement in participants suffering from CFS.

With respect to psychological adjustment, individuals with CFS showed more psychopathology than healthy, well-functioning people. As found previously (Fossey et al., 2004), they generally did not, however, experience more anxiety or depression than individuals with a diagnosed sleep disorder. Poor psychological functioning is comorbid with a number of medical conditions where sleep disorder and daytime fatigue are issues (e.g. DaCosta et al., 2002; Fruehwald, Loeffer-Stastka, Eher, Saletu, & Baumhackl, 2001). This pattern suggests that poor psychological functioning may be the consequence of living and coping with a chronic disorder.

The dramatically reduced quality of life scores for individuals with CFS, reflected in the findings of both the present study as well as a previous study carried out by our team (Fossey et al., 2004), support the interpretation that psychological adjustment problems are likely to be the consequence, rather than the cause, of CFS. It is not surprising that debilitating fatigue, characteristic of CFS, as well as non-refreshing, disrupted, and poor quality sleep, strongly undermine quality of life. It should be noted, however, that although similar levels of daytime fatigue may be experienced in other clinical disorders (e.g. multiple sclerosis, systemic lupus erythematosus, malignant disease), in other illnesses patients are generally not exposed to the rejection and stigmatization so frequently endured by those with chronic fatigue syndrome.

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