Original Paper

Neuropsychobiology

Neuropsychobiology 2007;56:40–46
DOI: 10.1159/000110727

Received: January 12, 2007
Accepted after revision: August 18, 2007
Published online: November 6, 2007

Sleep Quality Perception in the Chronic Fatigue Syndrome: Correlations with Sleep Efficiency, Affective Symptoms and Intensity of Fatigue

Daniel Neu[a, b] Olivier Mairesse[a] Guy Hoffmann[a] Amirouche Dris[d]
Luc J. Lambrecht[c] Paul Linkowski[b] Paul Verbanck[a] Olivier Le Bon[a]

[a]Sleep Laboratory, University Hospital Brugmann, Université Libre de Bruxelles, [b]Sleep Laboratory, University Hospital Erasme, Université Libre de Bruxelles, Brussels, and [c]Department of Internal Medicine, Biomed Flanders, Gent, Belgium; [d]Sleep Unit, Department of Oto-Rhino-Llaryngology, Kirchberg Hospital, Luxembourg, Luxembourg

Key Words
Sleep quality · Pittsburgh Sleep Quality index · Chronic fatigue syndrome · Affective symptoms

Abstract
Background/Aims: One of the core symptoms of the chronic fatigue syndrome (CFS) is unrefreshing sleep and a subjective sensation of poor sleep quality. Whether this perception can be expressed, in a standardized questionnaire as the Pittsburgh Sleep Quality Index (PSQI), has to our knowledge never been documented in CFS. Furthermore, correlations of subjective fatigue, PSQI, affective symptoms and objective parameters such as sleep efficiency are poorly described in the literature. ***Methods:*** Using a cross-sectional paradigm, we studied subjective measures like PSQI, Fatigue Severity Scale scores and intensity of affective symptoms rated by the Hamilton Depression and Anxiety scales as well as objective sleep quality parameters measured by polysomnography of 28 'pure' (no primary sleep and no psychiatric disorders) CFS patients compared to age- and gender-matched healthy controls. ***Results:*** The PSQI showed significantly poorer subjective sleep quality in CFS patients than in healthy controls. In contrast, objective sleep quality parameters, like the Sleep Efficiency Index (SEI) or the amount of slow-wave sleep did not differ significantly. Subjective sleep quality showed a correlation trend with severity of fatigue and was not correlated with the intensity of affective symptoms in CFS. ***Conclusion:*** Our findings indicate that a sleep quality misperception exists in CFS or that potential nocturnal neurophysiological disturbances involved in the non-recovering sensation in CFS are not expressed by sleep variables such as the SEI or sleep stage distributions and proportions.

Introduction

The chronic fatigue syndrome (CFS) is still a debated clinical entity with an estimated prevalence rate ranging from 0.2 to 0.7% [1]. CFS is a nosologically defined syndrome [2] of unknown etiology and pathogenesis. Furthermore, lifetime prevalence of a 6-month-long fatigue episode has been estimated to be up to 9% [3]. The American Sleep Disorders Association [4] and the American Psychiatric Association in its *Diagnostic and Statistical Manual of Mental Disorders* (DSM) [5] do not presently recognize CFS as a distinct clinical entity. During the last two decades, CFS has received several different confusing labels; it has also been called neurasthenia, a label first used in 1903 by Pierre Janet [6]. The *International Classification of Diseases* [7] defines neurasthenia as a neurotic disorder with muscle weakness accompanied by

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0302–282X/07/0561–0040$23.50/0

Accessible online at:
www.karger.com/nps

Dr. Daniel Neu, MD
Brugmann University Hospital U.L.B./V.U.B.
Sleep Laboratory U78 – Department of Psychiatry
4, Arthur Van Gehuchten Plaza, BE–1020 Brussels (Belgium)
Tel. +32 2 477 2554, Fax +32 2 477 2162, E-Mail daniel.neu@skynet.be

functional disorders (digestive or endocrinal), headaches and anxiety. The American Centers for Disease Control and Prevention criteria [2] define CFS as a more than 6-month-long fatigue, not being the result of ongoing exertion nor being alleviated by rest with an induced disability of 50% regarding usual daily activities.

Associated psychosomatic conditions such as fibromyalgia (FM) and irritable bowel syndrome (IBS) are very frequent in CFS [1]. There are similarities between IBS and CFS [8] and FM can be confused with CFS [1]. Wessley et al. [9] suggest that CFS, FM and IBS represent different manifestations of the same somatic and psychological disturbances.

Treatment options are varied and range from hormonal treatments (dehydroepiandrosterone, corticosteroids), immunotherapy and antidepressants to vitamins and alimentary complements. Besides cognitive behavioral therapy and graded aerobic exercise, no treatment option has shown evident reproducible benefits.

The current mainstream view about chronic fatigue is that the syndrome is either the result of an undetected primary sleep disorder, or is the psychosomatic expression of an anxiety or depression disorder, perhaps linked to a particular personality pattern. A more modern approach considers CFS as a multifactor clinical condition in a biopsychosocial model [1].

Sleep is at the crossroads of the suspected syndrome, as most patients complain of poor sleep quality and unrefreshing nights as mentioned above. Reports of sleep disturbances in CFS did not isolate a clear picture, largely because of different selection criteria, type of control group or characteristics of the recorded night (first night only, home recordings), which makes comparisons and reproducibility difficult. Several reports showed poor sleep efficiency (Sleep Efficiency Index, SEI) [10–14]. Some mentioned increased sleep onset latency (SOL) [10, 13], and increased number or duration [10, 12, 13] of intermittent awakenings. Rapid eye movements have been shown to decrease [10, 14] or increase [15]. A recent study reported reduced slow-wave sleep (SWS) but increased delta band power [16].

On the subjective side, the Pittsburgh Sleep Quality Index (PSQI) is one of the most used and well-validated questionnaires of subjective sleep quality [17]. It measures the average sleep quality of the last month, with higher scores indicating worse sleep. It has been applied in sleep disorders, general clinical conditions and psychosomatic medicine. Recently, a study using the PSQI showed no correlation of subjective and objective sleep quality in IBS [18]. These results were consistent with previously published results about sleep quality in IBS [19]. Assessment of sleep quality perception with the PSQI has to our knowledge never been published in CFS.

The objective of the present study was to test whether PSQI scores significantly express poorer sleep quality and whether this subjective sleep quality perception is correlated with objective sleep efficiency in CFS. Patients were compared to a group of healthy controls to confirm differences between the conditions. Descriptively, relations between PSQI and a panel of other objective sleep variables were tested. The relationships between PSQI severity of fatigue and intensity of affective symptoms were also measured.

To avoid potential biases in a sleep study, patients with primary sleep disorders such as sleep apnea-hypopnea syndrome (SAHS), periodic limb movement disorder (PLMD) or narcolepsy were excluded. Also, as mood and anxiety disorders are known to be associated with numerous sleep abnormalities, patients with such comorbid disorders were excluded. Patients presenting only with CFS are labelled 'pure' CFS.

The null hypothesis was that there would be no correlation relation between higher PSQI scores and decreased SEI. Considering the sample size, this study focuses on sleep efficiency measures, with and without SOL. The other objective parameters are analyzed descriptively.

Methods

Patients and Controls

During a 12-month period (from October 2005 to September 2006), patients with 'pure' CFS were selected prospectively among the population admitted to our sleep laboratory. The recruited CFS patients had fatigue and unrefreshing sleep as their main complaint. They were referred to the sleep unit by the medical department of another institution (tertiary care setting) after a full medical checkup. Center for Disease Control criteria were used for a first selection of CFS patients [2]: (1) clinically evaluated, unexplained or relapsing chronic fatigue – that is of new or definite onset – is not the result of ongoing exertion nor is it alleviated by rest, and results in the substantial reduction of previous levels of occupational, educational, social or personal activities; (2) concurrent occurrence of 4 or more of the following symptoms, all of which must have persisted or recurred during 6 or more consecutive months of illness and must not have predated the fatigue: self-reported impairment in short-term memory or concentration; sore throat; tender cervical or axillary lymph nodes; muscle pain; multijoint pain without joint swelling or redness; headaches of a new type, pattern or severity; unrefreshing sleep; postexertional malaise lasting more than 24 h; (3) exclusion of any active medical condition that may explain the presence of chronic fatigue; any previous condition which might explain fa-

tigue and which has not come to an end; substance abuse within 2 years prior to onset; severe obesity. In order to avoid potential overlaps with primary sleep or psychiatric disorders, further exclusion criteria were: (1) Apnea-Hypopnea Index or Periodic Limb Movement Index ≥5/h, clinical criteria for narcolepsy or idiopathic hypersomnia; (2) all DSM-IV axis I diagnoses. In unclear cases, rejection prevailed.

All patients had been free of neuropsychopharmacological treatment for at least 2 weeks prior to recording, and, in most cases, this period exceeded 3 months. Daytime napping was not allowed in the sleep unit. All patients in our lab completed questionnaires about lifestyle and drinking habits. Patients with a consumption of more than two units of alcohol per day were excluded.

Controls were locally recruited healthy volunteers. They were paid EUR 100 by private funding for their participation. Regular sleep-wake schedules were required and no working shifts were allowed. No significant somatic condition and no current or past mental disorder were allowed in the control group. Further exclusion criteria were identical to those of the patient group.

All patients and controls filled out a sleep diary 2 weeks prior to sleep recording to assess the regular sleep-wake schedule; they received a standard physical examination (D.N.), the structured clinical interview for DSM-IV [5] (D.N., G.H., O.L.) and psychometric assessment (D.N.).

All patients and controls gave written informed consent; the study was approved by the local ethics committee and conducted in accordance with the rules and regulations for the conduct of clinical trials stated by the World Medical Assembly in Helsinki.

Material

All participants admitted to the sleep unit were recorded for 2 consecutive nights without habituation. Recordings were performed between Mondays and Fridays. Participants were prepared for the recordings between 10 p.m. and 11 p.m. and allowed to retire when they wished. Morning arousal was spontaneous. Polysomnography included 3 electroencephalograms recorded from Fp2-A1, C4-A1, and O2-A1 sites, 2 electrooculograms, submental and bilateral anterior tibial electromyograms. Oral and nasal airflow were recorded by thermoresistors (Healthdyne® Technologies USA), and respiratory effort was measured by thoracic and abdominal belts (Pro-Tech® CT2™, Mukilteo, Wash., USA). Capillary oxygen saturation was monitored by photosensitive finger oximetry (Nonin® Flexi-Form® II 7000A, Nonin Medical Inc., Minneapolis, Minn., USA, and LINOP® Adt, Masimo Corp., Irvine, Calif., USA).

Polysomnography

All recordings were randomly analyzed by one of two well-trained technicians, amidst other clinical work and without knowledge of the study goals, on 21-inch screens displaying 30-second polysomnogram epochs (Respironics Inc.™ Alice® 4 and 5, Murrysville, Pa., USA). Respiratory events were reviewed visually by the technicians. Classical criteria were used for sleep stage scoring [20]. Interrater reliability (kappa) exceeded 0.89 for all variables.

SOL was defined as the time between lights out and the first period of stage 2. Wake time did not include sleep latency. SEI 1 was defined by the total sleep time/time in bed ratio. SEI 2 was defined by the total sleep time/period of sleep time ratio. Non-rapid eye movement sleep included sleep stages 1–4. Rapid eye movement sleep latency was defined as the time between the first epoch of stage 2 and the first of rapid eye movement sleep. Light sleep was the sum of stages 1 and 2. SWS was the sum of stages 3 and 4. The ratios are expressed in percentages. An episode of apnea was defined as more than an 80% reduction in airflow for at least 10 s during sleep. Hypopnea was defined as a 50–80% reduction of airflow amplitude accompanied by either a 3% or greater reduction in oxygen saturation or an arousal. Microarousals were defined according to the American Sleep Disorders Association criteria [21]. The Microarousal Index (MAI) represented the number of microarousals per hour of sleep.

PSQI and Fatigue Scale

All participants answered the self-reporting questionnaires on the first day of their stay in our unit at the same daytime (between 5 p.m. and 7 p.m.) before their first night of polysomnographic recording.

Scoring of the PSQI was performed according to the guidelines provided by the authors [17]. The 19 items are grouped into 7 component scores, each weighted equally on a scale from 0 to 3. These components are subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication and daytime dysfunction. The component scores were then summed to give the global PSQI score. In validation studies, a global PSQI score >5 indicates that a subject is having severe difficulties in at least 2 areas, or moderate difficulty in more than 3 areas [17].

The Fatigue Severity Scale (FSS) is a self-report instrument used to assess levels of fatigue and its effect on daily functioning. The FSS was first used on individuals with multiple sclerosis and systemic lupus erythematosus. It has later been used in studies on obstructive sleep apnea, aerobic exercise [22], fatigue, obesity, Parkinson disease, hepatitis C infection or CFS [23].

Affective Symptoms Scales

All patients completed the 13-item short form of the Beck Depression Inventory (BDI) on the first day of their stay in our laboratory before the first night of polysomnography between 5 p.m. and 7 p.m. All subjects were rated with the 21-item Hamilton Depression Rating Scale (HAMD-21) and the Hamilton Anxiety Scale (HAMA) between 11 a.m. and 13 p.m. by the same interviewer (D.N.) on the second day of their stay in our laboratory after their first night of polysomnographic recording.

Statistics

All variables in each of the groups were compatible with the use of parametric tests, except for the PSQI subscales. Between-group comparisons involving continuous data were computed using MANOVAs with Bonferroni correction: one MANOVA was performed for the sleep parameters and another one for the psychological tests. When equality of variances was not met, Mann-Whitney nonparametric tests were used. Association between continuous variables within the CFS group was tested using the Pearson product-moment r. Hypothesis tests were two-sided and carried out at the 5% significance level. Trends are noted at a 5–10% level. All results are expressed as mean ± standard error of the mean. The statistical analyses were computed using SPSS 10® (SPSS Inc., Chicago, Ill., USA).

Table 1. Descriptive variables and objective sleep parameters

Variable	CFS (n = 28)	Controls (n = 12)	p
Age, years	34.2 ± 9.2	32.3 ± 9.6	NS[a]
BMI	23.1 ± 4.1	21.3 ± 2.0	NS[a]
TIB, min	508.6 ± 58.0	485.2 ± 50.5	NS[a]
SPT, min	472.1 ± 59.4	457.9 ± 50.7	NS[a]
TST, min	433.1 ± 71.8	406.1 ± 32.5	NS[a]
SOL, min	26.5 ± 15.6	21.2 ± 11.3	NS[a]
SEI 1, %	84.6 ± 8.2	84.1 ± 5.9	NS[a]
SEI 2, %	91.4 ± 7.2	89.1 ± 6.2	NS[a]
WASO, %	8.6 ± 7.2	10.9 ± 6.1	NS[a]
LS, %	53.9 ± 11.5	54.2 ± 8.6	NS[a]
SWS, %	24.0 ± 11.6	22.0 ± 11.8	NS[a]
NREMS, %	77.9 ± 7.5	76.2 ± 8.3	NS[a]
REMS, %	13.6 ± 6.1	13.3 ± 5.9	NS[a]
RL, min	83.6 ± 51.9	80.4 ± 64.6	NS[a]
AHI (per h)	2.3 ± 2.4	1.1 ± 1.3	0.095[b]
MAI	30.8 ± 18.5	11.9 ± 6.1	0.001[b]

Values are presented as means ± standard deviation. Ratios are presented as means ± standard deviation and expressed as percentages.

TIB = Time in bed; SPT = sleep period time; TST = total sleep time = SPT – WASO; SEI 1 = TST/TIB; SEI 2 = TST/SPT; WASO = wake after sleep onset; LS = light sleep = sleep stages 1 and 2; REMS = rapid eye movement sleep in percent of SPT; RL = REM sleep latency; AHI = Apnea-Hypopnea Index.

[a] MANOVA; [b] Mann-Whitney.

Table 2. Comparison of subjective parameters: PSQI, FSS, HAMA, HAMD, BDI

Variable	CFS (n = 28)	Controls (n = 12)	p (Mann-Whitney)
PSQI global score	9.54 ± 4.0	2.42 ± 1.2	0.001
Sleep quality	1.7 ± 0.7	0.7 ± 0.5	0.001
Sleep latency	1.8 ± 1.0	0.5 ± 0.6	0.001
Sleep duration	0.7 ± 1.0	0.2 ± 0.4	NS
Sleep efficiency	1.0 ± 1.1	0.1 ± 0.3	0.017
Sleep disturbance	1.5 ± 0.7	0.7 ± 0.4	0.004
Use of medication	0.8 ± 1.3	0.0 ± 0.0	NS
Daytime dysfunction	2.0 ± 0.7	0.2 ± 0.4	0.001
FSS mean score	6.2 ± 0.8	1.7 ± 1.1	0.001
HAMA	17.2 ± 4.6	3.1 ± 1.8	0.001
HAMD-21	10.2 ± 3.9	1.7 ± 1.2	0.001
BDI-13	9.1 ± 5.5	0.3 ± 0.6	0.001

Scores are presented as means ± standard deviation.

Results

Our sample included 28 'pure' CFS female patients and 12 female controls. Table 1 shows descriptive and polysomnographic variables. Sleep data examined in statistical analyses were from the second recorded night only, in order to avoid potential first-night effects [24], in particular in the CFS [25]. Age was not significantly different between CFS patients and healthy controls (34.2 ± 9.2 years vs. 32.3 ± 9.6 years).

As equality of variances was not met for the MAI, the variable was removed from the MANOVA on objective sleep variables. No significant difference was evidenced between groups. The MAI was shown to be higher in the CFS than in the control group using the Mann-Whitney U test (p = 0.001).

Mann-Whitney tests showed significant differences between patients and controls for all global scores in subjective measurements (p = 0.001 in each case). PSQI subscales showed significantly higher scores (worse sleep quality) in the patient group for sleep quality, sleep latency, sleep efficiency, sleep disturbance and daytime dysfunction. Sleep duration and use of medication were not statistically distinct (table 2).

Correlations between the PSQI and its subscales, and objective sleep quality parameters, including MAI, were not significant in the patient group (r = –0.195; r = –0.161). Correlations between the FSS and objective sleep measures were not significant either. Correlations between the HAMA and sleep measures showed a trend for SWS (r = –0.364, p = 0.057). The BDI was correlated with sleep efficiency 1 (r = –0.391; p = 0.040), SOL (r = 0.478; p = 0.010) and a trend for SWS (r = –0.359; p = 0.061).

Not surprisingly, average correlations appeared between the scales measuring affective states. The same comparisons in the healthy control group showed quite weak associations, except for links between both Hamilton scales (data not shown).

Discussion

This study compared objective and subjective parameters of sleep as well as the affective state of 28 female 'pure' CFS patients and 12 female healthy controls. The main objective was the assessment of relationships between sleep efficiency and subjective evaluation of sleep quality. Several other analyses were performed descriptively using other objective sleep parameters and subjective scales other than the PSQI.

Sleep efficiency, whether including the SOL or not, was not shown to differ significantly between the CFS and the control group. Comparisons on sleep quality perception (PSQI) unambiguously showed poorer ratings in CFS patients than in controls. A mismatch seems thus to be present between the subjective perception and the objective analysis of CFS sleep. The possibility of a misperception had also previously been mentioned in an interesting study about twins who were discordant for CFS [26].

As Elsenbruch et al. [19] proposed in a similar paper about IBS, this mismatch may mean either that (1) the perception of sleep quality is affected by the same mechanisms that trigger CFS: such a mechanism may lower patients' perceptual threshold for both CFS and sleep evaluation; (2) the attention paid to internal stimuli in general may be affected, so that slight deviations from normalcy, such as a brief awakening or perception of fatigue, are more likely to be remembered and interpreted as an abnormality; (3) anxiety creates or enhances a response bias towards reporting both CFS and sleep problems, as the influence of psychological states on perception have been emphasized. Insomniacs are known to underestimate their sleep, whereas healthy subjects tend to overestimate it [27, 28]. In other words, these biases can either be of psychological or biological origin, if we accept a Cartesian division of mind and body.

Because of sample size issues, all analyses except for the correlations between the PSQI and objective sleep efficiency measures are to be considered descriptive, as has been said above. The substantial quantitative differences in microarousals observed here between patients and controls were also described in another study by our group in a distinct group of CFS patients [29]. What is particularly striking is that there is no identifiable cause for triggering these microarousals in CFS, in contrast to microarousals in SAHS, PLMD, or experimental noise exposure disturbances, for example. In general, microarousals can be related to wake-triggering phenomena such as changes in airflow and blood gasometry in SAHS or myoclonias in PLMD. Furthermore, an increased number of microarousals in primary sleep disorders is generally related to a relative and significant reduction of SWS. No such reduction of SWS was apparent here or in our retrospective study [29]. Thus, respiratory or subcortical events may explain these microarousals in other conditions, but there is no identifiable cause for them in CFS. Microarousals can thus partially account for the nonrecovering and unrefreshing sleep sensations in CFS.

Miscellaneous subjective measures, on the other hand, showed more daytime fatigue (FSS), more depression (HAMD and BDI) and more anxiety (HAMA) in the CFS group. Most of the recent research studies on CFS tend to consider CFS as distinct from major depressive disorder when considering clinical diagnostic criteria [30, 31], but also when considering opposite hypothalamic-pituitary-adrenal axis regulation profiles [32] and diminished SWS in major depressive disorder [33–35]. The findings in our sample, where duration and proportion of SWS showed no significant difference compared to controls, confirm these differences. Although no patient in the sample could be diagnosed with DSM-IV major depression, depression ratings were not negligible. Statistical trends were even found for a negative association between SWS and intensity of depression (HAMD and BDI). However, despite this relatively high intensity of depression, SWS was not reduced as a whole. Also, intensity of depression was not associated with intensity of fatigue.

Although both the MAI and the PSQI differed between the patient and the control groups, they were not correlated with each other. A high level of microarousals is therefore not translated into poorer sleep quality perception.

The substantially more elevated scores on the PSQI found in CFS patients in comparison to controls indicate that the PSQI can also be used in CFS as a clinical routine measure for the severity of patients' complaints about sleep quality.

There are some limitations that have to be considered. The absence of significant differences in the remaining objective sleep parameters could be due to the way these variables are assessed. Sleep stages, proportions and sleep architecture (classical scoring) are global concepts with limited meanings. The main difficulty arises from the usual 30-second epoch staging, which may hide short-duration events. Different underlying physiological or pathological brain processes could express themselves, according to the used sleep staging criteria, with the same sleep stage proportions [36]. Quantitative approaches like sleep EEG power spectral analysis and analysis of sleep microstructure, notably the cycling alternating pattern, may, in the future, prove more promising when seeking for sleep-related abnormalities that could account for the daytime symptoms in CFS [16]. However, increases in specific power bands (ultraslow, or delta) cannot presently be related to sleep efficiency or refreshing sleep.

This being a sleep study, we thought it was crucial to isolate patients not suspected of suffering from comorbid disorders which may interfere with sleep, such as SAHS,

PLMD or major depression. Our sample is thus superselected. This means that the present patient group fulfills all the Center for Disease Control criteria but that all patients with Center for Disease Control criteria may not display the present findings. The conclusions as such cannot therefore be generalized to them. It is, however, our conviction that including patients with identifiable sleep disorders or disorders well known to be associated with sleep anomalies only confuses the matter and we advocate the analysis of 'pure' CFS in sleep studies at least.

In conclusion, our findings indicate either that a sleep quality misperception may be present in CFS or that the neurophysiological disturbances involved in the nonrecovering sensation in CFS are not expressed by sleep variables such as SEI or sleep stage distributions and proportions. Future studies investigating sleep in CFS should perhaps focus upon sleep microstructure and quantitative sleep EEG measurements. The present findings are reinforced by the strict selection criteria used here for CFS patients, where confounding sleep disorders such as PLMD or SAHS as well as comorbid axis I diagnoses were excluded, while adaptation issues to the lab were reduced by using only results from the second recorded night.

Acknowledgments

We would like to express our gratitude to Julie Martina for her devoted work during the data acquisition and recording. We would also like to thank Robert Moutrier, MD, for reviewing the manuscript. D.N. was supported by a research grant from the National Funding for Scientific Research from the Ministry of Research, Culture and Superior Education of the Grand-Duchy of Luxembourg. P.L. was supported by the National Funding for Scientific Research (FNRS), Belgium. O.L. was supported by SOMALCPE, a private fund dedicated to research in psychiatric neurosciences and sleep medicine.

References

1 Maquet D, Demoulin C, Crielaard JM: Chronic fatigue syndrome: a systematic review. Ann Readapt Med Phys 2006;49:337–347, 418–427.
2 Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbings JG, Komaroff A, the International Chronic Fatigue Syndrome Study Group: The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med 1994;121:953–959.
3 Scott LV, Medbak S, Dinan TG: Blunted adrenocorticotropin and cortisol responses to corticotropin-releasing hormone stimulation in chronic fatigue syndrome. Acta Psychiatr Scand 1998;97:450–457.
4 American Sleep Disorders Association: International Classification of Sleep Disorders, Revised. Rochester, American Sleep Disorders Association, 1997.
5 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 4. Washington, American Psychiatric Association Press, 1994.
6 Janet P: Obsessions and Psychasthenia. Paris, Alcan, 1903.
7 World Health Organization: International Classification of Diseases, ed 10. Geneva, World Health Organization, 1990.
8 Gomborone JE, Gorard DA, Dewsnap PA, Libby GW, Farthing MJ: Prevalence of irritable bowel syndrome in chronic fatigue. J R Coll Physicians Lond 1996;30:512–513.
9 Wessely S, Nimnuan C, Sharpe M: Functional somatic syndromes: one or many? Lancet 1999;354:936–939.
10 Whelton CH, Salit I, Moldofsky H: Sleep, Epstein-Barr, virus infection, musculoskeletal pain and depressive symptoms in chronic fatigue syndrome. J Rheumatol 1992;19:6:939–943.
11 Morris R, Sharpe M, Sharpley AL, Cowen PJ, Hawton K, Morris J: Abnormalities of sleep in patients with the chronic fatigue syndrome. BMJ 1993;306:1161–1164.
12 Sharpley A, Clements A, Hawton K, Sharpe M: Do patients with 'pure' chronic fatigue syndrome (neurasthenia) have abnormal sleep? Psychosom Med 1997;59:592–596.
13 Fischler B, Le Bon O, Hoffmann G, Cluydts R, Kaufman L, De Meirleir K: Sleep anomalies in the chronic fatigue syndrome. Neuropsychobiology 1997;35:115–122.
14 Stores G, Fry A, Crawford C: Sleep abnormalities demonstrated by home polysomnography in teenagers with chronic fatigue syndrome. J Psychosom Res 1998;45;1:85–91.
15 Ball N, Buchwald D, Schmidt D, Goldberg G, Ashton S, Armitage R: Monozygotic twins discordant for chronic fatigue syndrome. Objective measures of sleep. J Psychosom Res 2004;56:207–212.
16 Guilleminault C, Poyares D, Rosa A, Kirisoglu C, Almeida T, Lopes MC: Chronic fatigue, unrefreshing sleep and nocturnal polysomnography. Sleep Med 2006;7:513–520.
17 Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213.
18 Heitkemper M, Jarrett M, Burr R, Cain KC, Landis C, Lentz M, Poppe A: Subjective and objective sleep indices in women with irritable bowel syndrome. Neurogastroenterol Motil 2005;17:523–530.
19 Elsenbruch S, Harnish MJ, Orr WC: Subjective and objective sleep quality in irritable bowel syndrome. Am J Gastroenterol 1999;94:2447–2452.
20 Rechtschaffen A, Kales A (eds): A Manual of Standardized Terminology Techniques and Scoring System for Sleep Stages of Human Subjects. Washington, US Government Printing Office, 1968.
21 American Sleep Disorders Association: EEG arousals: scoring rules and examples. A preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. Sleep 1992;15:174–184.
22 Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD: The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121–1123.
23 Olson LG, Ambrogetti A, Sutherland DC: A pilot randomized controlled trial of dexamphetamine in patients with chronic fatigue syndrome. Psychosomatics 2003;44:38–43.
24 Agnew HW, Webb WB, Williams RL: The first-night effect: an EEG study of sleep. Psychophysiology 1966;2:263–266.
25 Le Bon O, Minner P, Van Moorsel C, Hoffmann G, Gallego S, Lambrecht L, Pelc I, Linkowski P: First-night effect in the chronic fatigue syndrome. Psychiatry Res 2003;120:191–199.

26 Watson NF, Kapur V, Arguelles LM, Goldberg J, Schmidt DF, Armitage R, Buchwald D: Comparison of subjective and objective measures of insomnia in monozygotic twins discordant for chronic fatigue syndrome. Sleep 2003;26:324–328.
27 Coates TJ, Killen JD, Silverman S, George J, Marchini E, Hamilton S, Thoresen CE: Cognitive activity, sleep disturbance, and stage specific differences between recorded and reported sleep. Psychophysiology 1983;20:243–250.
28 Carskadon MA, Dement WC, Mitler MM, Guilleminault C, Zarcone VP, Spiegel R: Self-reports versus sleep laboratory findings in 122 drug-free subjects with complaints of chronic insomnia. Am J Psychiatry 1976;133:1382–1388.
29 Le Bon O, Neu D, Valente F, Linkowski P: Paradoxical NREMS distribution in 'pure' chronic fatigue patients: a comparison with sleep apnea-hypopnea patients and healthy control subjects. J Chronic Fatigue Syndr, in press.
30 Caplan C: Chronic fatigue syndrome or just plain tired? CMAJ 1998;159:519–520.
31 Powell R, Dolan R, Wessely S: Attributions and self-esteem in depression and chronic fatigue syndromes. J Psychosom Res 1990;34:665–673.
32 Demitrack MA, Crofford LJ: Evidence for and pathophysiologic implications of hypothalamic-pituitary-adrenal axis dysregulation in fibromyalgia and chronic fatigue syndrome. Ann NY Acad Sci 1998;840:684–697.
33 Hubain P, Le Bon O, Vandenhende F, Van Wijnendaele R, Linkowski P: Major depression in males: effects of age, severity and adaptation on sleep variables. Psychiatry Res 2006;145:169–177.
34 Adrien J: Neurobiological bases for the relation between sleep and depression. Sleep Med Rev 2002;6:341–351.
35 Jones D, Gershon S, Sitaram N, Keshavan M: Sleep and depression. Psychopathology 1987;20(suppl 1):20–31.
36 Rechtschaffen A: Current perspectives on the function of sleep. Perspect Biol Med 1998;41:359–390.