How Significant are Primary Sleep Disorders and Sleepiness in the Chronic Fatigue Syndrome?

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In order to study both the prevalence of Primary Sleep Disorders (PSD) and sleepiness, and their association to the Chronic Fatigue Syndrome (CFS), 46 unselected outpatients (34 women, mean age 36.5) were examined clinically and underwent two nights of all-night polysomnography and multiple sleep latency tests (MSLT). Forty-six percent presented with a Sleep Apnea/Hypopnea Syndrome Index (AHI>=5), 5% with a Periodic Limb Movements syndrome. No subject received a diagnosis of Narcolepsy or Idiopathic Hypersomnia. Thirty percent showed the presence of objective sleepiness as measured by MSLT<10 minutes. Objective and subjective measures of sleepiness were not associated with CFS, nor with the double diagnosis of CFS and a PSD. The presence of PSD or sleepiness was not associated with any of the clinical scales that were used to measure anxiety, depression, somatisation, physical or mental fatigue, or functional status impairment. Fifty-four percent of CFS patients had no PSD, and 69% no sleepiness. These patients could not be distinguished clinically from patients having a PSD or from those with sleepiness. Therefore, it is unlikely that CFS is simply a somatic expression of any PSD observed in our sample or of sleepiness per se.

CURRENT CLAIM: Primary sleep disorders cannot be reduced to a somatic expression of a primary sleep disorder or of sleepiness.

Fatigue is a decline in performance in prolonged or repeated tasks. It can be subdivided into physical fatigue, the failure to sustain power output, and mental fatigue, which refers to the decreased ability to perform mental tasks (Edwards, 1981). Fatigue is also a negative sensation, often described by patients in association with depression, general malaise or pain. Fatigue can be distinguished from weakness, which is the failure to generate force, and from sleepiness, which is the tendency to fall asleep during daytime.

Chronic fatigue is a severely disabling condition, affecting between 2 to 130 per 100,000 patients in a primary care setting (Wessely, 1995). The diagnostic criteria of Chronic Fatigue Syndrome (CFS) include fatigue lasting more than six months, multiple complaints about somatic and neuropsychological dysfunction, as well as a substantial reduction in occupational, social or personal activities (Kruesi et al., 1989). The etiology of CFS is not known and speculations range from viral infections to immunologic dysfunction, to psychiatric and sleep disorders (for a review, see Fischler, 1999).

Sleep dysregulation remains among the most promising hypotheses. The implication of sleep in the CFS is suggested by: 1) post-exertional fatigue, myalgia and neuropsychological impairment that are often consequences of sleep deprivation (Moldofsky et al., 1975; Horne, 1988; Myles, 1985); 2) frequent subjective sleep complaints by CFS patients of poor and unrefreshing sleep starting after illness onset (Komaroff, 1991); and 3) objective sleep dysfunction, with reduced sleep efficiency, longer sleep onset, reduction of REM sleep, excess wake time (Whelton et al., 1992; Morriss et al., 1997), and a reduction of Stage 4 sleep (Fischler et al., 1997) among patients having CFS. REM latency among CFS patients was not shown to differ from controls (Whelton et al., 1992; Morriss et al., 1997). Studies on alpha intrusion in NREM sleep in CFS have provided conflicting results (Whelton et al., 1992; Morriss et al., 1997; Moldofsky, 1993).

Sleep complaints and objective abnormalities are thus prevalent in CFS and have been found to be associated with functional disability in one study (Morriss et al., 1997). It is unclear whether these abnormalities contribute significantly to the pathophysiology of CFS. Perhaps CFS could be reduced to a somatic expression of a primary sleep disorder (PSD), such as sleep apnea/hypopnea syndrome (SAHS), periodic limb movements (PLM), narcolepsy or idiopathic hypersomnia. The possible contribution of these syndromes to CFS symptomatology is not yet well established. Previous studies exploring such phenomena have not directly examined the relationship between PSD and CFS as their primary objective (Whelton et al., 1992; Manu et al., 1994; Krupp et al., 1993; Buchwald et al., 1994). Sleepiness, on the other hand, is not considered to be a primary sleep disorder anymore, but rather a symptom common to many disorders (ASDA, 1990). Sleepiness was not found to be predictive of CFS in one study (Lichstein et al., 1997). However, many patients confuse sleepiness with fatigue, and it remains interesting to compare the association of both symptoms within CFS.

The present study attempts to: 1) measure the global prevalence of PSD and sleepiness in patients affected by CFS; 2) assess whether sleepiness is a characteristic of patients presenting with both CFS and PSD; and 3) measure whether PSD or sleepiness are associated with chronic fatigue.
symptoms. Internationally accepted clinical criteria for chronic fatigue were employed to enroll a group of consecutive subjects. The International Classification of Sleep Disorders (ASDA, 1990) was used to classify sleep disorders, except for sleep respiratory disorder and periodic limb movement disorder, where objective measurements by all-night polysomnographies were used for their better diagnostic precision.

**METHODS**

**Patients**

Fifty-three consecutive outpatients with the primary complaint of fatigue (mean age=36.38.6 yrs; 36 women [68%]) were diagnosed using a structured interview for Oxford CFS criteria (Sharpe et al., 1991) in a tertiary care setting (fatigue clinic). All subjects also fulfilled the more recent International Chronic Fatigue Syndrome Study Group criteria (Fukuda et al., 1994). Exclusion criteria included current drug or alcohol abuse or dependence, bipolar disorder, schizophrenia and other psychotic disorders. Patients were not excluded on the basis of comorbid anxiety, affective disorder or somatization disorder. All were free of psychotropic drugs for at least two weeks at the time of polysomnographic recording and in most cases this period exceeded three months. All subjects gave informed consent. There were no refusals nor did any of the subjects drop out.

**Methods**

Several aspects of fatigue and functional impairment were measured. To assess psychiatric disorders, patients were interviewed by a senior psychiatrist (B.F.), with the Structured Clinical Interview for the DSM-III-R (APA, 1987), with a validated somatisation scale designed especially for CFS (Derogatis, 1977) and general somatisation scale (SOMGEN), and the Clinical Interview for the DSM-III-R (APA, 1987), with measures of anxiety and depression were performed by the Hamilton anxiety scale (Hamilton, 1959) and the 17-item Hamilton depression rating scale (Hamilton, 1967), respectively. Somatisation was assessed using the SCL-90 (Dorogatis, 1977) and a validated somatisation scale designed especially for CFS with a 5 Likert score (SOMCFS) (Fischler et al., 1997). Fatigue assessment was performed using the Checklist of Individual Strength (CIS) (Vercoulen et al., 1994), a reliable and validated self-rating scale designed to measure four dimensions of fatigue, namely subjective experience of fatigue, concentration, motivation, and physical activity. Functional impairment was assessed with the Sickness Impact Profile total score (SIP) (Bergner et al., 1981). The Finger Tapping Test (Halstead, 1947) measures psychomotor activity and was found in a post hoc analysis (Michiels et al., 1996) to be the most discriminant test available to detect mental and physical fatigue. The number of taps made with the index finger of each hand were recorded. A practice trial of 5 sec was followed by three consecutive trials of 10 sec with each hand. The number of taps for each of the trials and the mean number of taps are calculated for each hand. Subjective sleepiness was assessed with the Stanford Sleepiness Scale (SSS) (Hoddes et al., 1973). It was performed immediately before going to bed (SSS-1) and immediately after the awakening (SSS-2). The American College of Rheumatology criteria (Wolfe et al., 1990) were used for the diagnosis of Fibromyalgia (FM). A structured interview based on the International Classification of Sleep Disorders (ASDA, 1990) was used to assess Narcolepsy, Idiopathic Hypersomnia, and Excessive Daytime/Pathological Sleepiness.

**Polysomnography**

Patients spent a first night in the lab for habituation where they were installed as for polysomnography, but data were not recorded. This was immediately followed by two all-night polysomnographies. Patients were prepared for the recordings between 10:00 and 11:00 p.m. and were allowed to retire when they wished (Goodnight Time). They were awakened around 7:30 a.m., had they not arisen spontaneously (Good Morning Time). Polysomnography involved an electroencephalogram recorded from C4-A1, C3-A2, Fpz2-A1, Fpz1-A2, O2-A1, O1-A2 sites, as well as an electrooculogram, submental and anterior tibial electromyograms (randomly on the left or right leg). Oral and nasal airflow (thermistors at the nose and the mouth), respiratory effort (thoracic and abdominal belt) and arterial oxygen saturation were recorded on the first night only. Sleep data were recorded on a Nicolet Ultrasom and scored visually by trained sleep technicians in 30-sec epochs according to standard criteria (Rechtschaffen and Kales, 1968). The technicians were blinded to the aims of the study and scoring for patients in this study was incorporated into groups of readings made as part of routine clinical activities. The inter-rater reliability (kappa) for visual scoring, measured in a previous study in our lab (Le Bon et al., 1997), exceeded 0.90 for all variables.

Sleep apnea episodes were defined as the cessation of airflow (more than 80% obstruction) for at least 10 sec during sleep. Hypopneic episodes were defined as a 50% to 80% reduction of airflow amplitudes accompanied by either a 3% or greater reduction in oxygen saturation or an arousal, for at least 10 sec. Apeas were defined as obstructive when the cessation of airflow was accompanied by thoracic or abdominal efforts to breathe, and of central origin when these efforts were not present. A small number of sleep apneic/hypopneic episodes is often encountered in controls. A maximum of five apneas or hypopneas per hour (Apnea-Hypopnea Index, or AHI) was the threshold for normality (Guilleminault and Dement, 1978).

Periodic Limb Movements during sleep (PLMs) (Montplaisir and Godbout, 1989) are defined as rhythmic extensions of the big toe and dorsiflexions of the ankle, sometimes with flexions of the knee and hip, each movement lasting 0.5 to 5.0 sec and occurring every 20 to 40 sec. A minimum of three episodes of at least 30 bursts are required for the classification as positive in this study. Very few episodes are expected in controls.

Multiple Sleep Latency Tests (MSLT) (Carskodon and Dement, 1982) are invitations to sleep at regular intervals (11 a.m., 1 p.m., 3 p.m., 5 p.m.) for 20-min periods. The MSLT took place between the two all-night polysomnographies. The
sleep criteria for narcolepsy applied were: (a) two out of four MSLT positive for REM sleep, and (b) a mean Sleep Onset of less than five minutes. REM sleep is not expected during a MSLT and its presence is consistent with Narcolepsy.

**Statistics**

The Apnea-Hypopnea Index (AHI) variable was logtransformed to achieve normality. Relationships between variables were evaluated using the Pearson correlation test. Chi-square (or Fisher’s exact test when appropriate) were used for two-by-two comparisons between nominal groups. Between-group comparisons involving continuous data were computed using Student’s t-tests for unpaired groups. Logistic regression was used for binary outcomes and stepwise regression was used for dependent ratio measures. The statistical analyses were computed using SPSS 6.1.

### RESULTS

Data from 46 of the 53 enrolled patients were entered into analyses; data from seven were excluded (five because of protocol breaches caused by staffing limitations; one failure of the automated data acquisition system; one onset of acute gastrointestinal illness). The subgroup of 46 patients did not differ significantly in age, gender or clinical characteristics from the original group (data not shown).

The population was predominantly female (74%). Age at onset of CFS was 29.9 (8.6); age at the time of study was 36.5 (8.7). Acute onset, as recollected by patients, was present in 10 cases (22%). Twenty-two patients (48%) had a comorbid diagnosis of fibromyalgia. Comorbid psychiatric disorders included 6 Current Major Depressive Disorder, 20 Past Major Depressive Disorder, 23 Generalized Anxiety Disorder and 6 Panic Disorder. Twenty-nine subjects (63%) had at least one past or present psychiatric diagnosis.

Sleep data from the first recorded night were evaluated statistically. The second night data was not examined due to potential influence of the MSLT conducted between the two nights of recording. Twenty-one patients (46%) had an AHI>=5 (mean 13.8; median 8.9) but only three patients (7%) had an index above 20 (see Table 1 for stratification). The same calculations were performed using higher thresholds (AHI>=10 and AHI>=20) with no significant differences. Obstructive apneas predominated (94%) among patients having an elevated AHI score. More than two episodes of Periodic Limb Movement were present in two patients (4.3%); and, in these two individuals, PLM occurred concomitantly with an AHI>=5. No subject met clinical (ICSD) or sleep inclusion criteria for Narcolepsy, and no patient was positive for HLA DR2 (although three patients were positive for HLA DQW1). No patient met clinical (ICSD) criteria for Idiopathic Hypersomnia. Thus, the use of standard definitions and thresholds showed that a total of 21 patients (46%) met the definition of at least one PSD. Descriptive sleep variables are detailed in Table 1. Stratification of AHI and of mean MSLT are shown in Table 2.

### Analyses

No association was found between PSD and measures of sleepiness by logistic regression with PSD as dependent variable and MSLT latency, SSS-1 or SSS-2 as predictors; or with chi-square tests between PSD and MSLT<10 minutes; or by stepwise linear regression between AHI score and mean MSLT, SSS-1 or SSS-2.

Logistic regression analyses were also performed between PSD and MSLT<10 minutes as dependent variables and scales measuring chronic fatigue symptoms as predictors. Independent variables included anxiety and depression scales (HAM-A and HAM-D), somatisation items (SOMGEN and SOMCFS), measures of fatigue (CIS1-4), sickness impact profile (SIP-T) and the finger tapping test. Presence of at least one psychiatric diagnosis and fibromyalgia were also included in the analysis, due to the frequent association of these syndromes with CFS. No significant associations were observed for the analyses with PSD. Analyses using MSLT<10 minutes showed a significant result for the

### Table 1: Descriptive Sleep Data

<table>
<thead>
<tr>
<th>n = 46</th>
<th>Sleep Variables</th>
<th>Standard Deviations</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIB (min)</td>
<td>441.1</td>
<td>45.7</td>
</tr>
<tr>
<td>SPT (min)</td>
<td>408.2</td>
<td>49.2</td>
</tr>
<tr>
<td>TST (min)</td>
<td>330.7</td>
<td>70.2</td>
</tr>
<tr>
<td>Sleep Efficiency Index (%)</td>
<td>74.7</td>
<td>12.3</td>
</tr>
<tr>
<td>Stage Shifts (#)</td>
<td>201.1</td>
<td>47.4</td>
</tr>
<tr>
<td>Sleep Onset (min)</td>
<td>31.7</td>
<td>18.9</td>
</tr>
<tr>
<td>Stage 1 (min)</td>
<td>58.0</td>
<td>23.8</td>
</tr>
<tr>
<td>Stage 2 (min)</td>
<td>156.1</td>
<td>50.7</td>
</tr>
<tr>
<td>Stage 3 (min)</td>
<td>40.2</td>
<td>18.2</td>
</tr>
<tr>
<td>Stage 4 (min)</td>
<td>36.6</td>
<td>27.3</td>
</tr>
<tr>
<td>SWS (min)</td>
<td>76.8</td>
<td>31.1</td>
</tr>
<tr>
<td>REM sleep (min)</td>
<td>39.1</td>
<td>16.3</td>
</tr>
<tr>
<td>REM Latency (min)</td>
<td>106.8</td>
<td>78.8</td>
</tr>
</tbody>
</table>

TIB: Time in bed; SPT: Sleep period time; TST: Total sleep time; SWS: Slow wave sleep.

### Table 2: Stratification of Sleep Apneas and MSLT

<table>
<thead>
<tr>
<th>Total Combined</th>
<th>Sleep Apnea/Hypopnea (AHI), more severe cases to the right</th>
<th>Mean Sleep Latency (min), more severe cases to the right</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;5</td>
<td>25 (54 %)</td>
</tr>
<tr>
<td></td>
<td>≥5-&lt;10</td>
<td>14 (30%)</td>
</tr>
<tr>
<td></td>
<td>≥10-&lt;15</td>
<td>2 (4 %)</td>
</tr>
<tr>
<td></td>
<td>≥15-&lt;20</td>
<td>2 (4 %)</td>
</tr>
<tr>
<td></td>
<td>≥20</td>
<td>3 (7 %)</td>
</tr>
</tbody>
</table>

Total: numbers and percentages calculated each for each subset on 46 patients; Combined: the addition of numbers and percentages starting from the most severe cases.
multivariate analysis (Wald: 6.65; \(p=0.009\)). Fibromyalgia was the only associated independent variable (\(p=0.0178\)). This association between short MSLT and paucity of fibromyalgia was further tested in a contingency table (Fisher’s exact test: \(p=0.0256\)) and with MSLT evaluated as a continuous variable (\(t\)-test: \(p=0.022\)). A description of these data is shown in Table 3. Stepwise regression analyses were also performed using respectively AHI, the primary source of PSD, and SSS-1 and 2 with the same independent variables. No comparison provided significant results (data not shown).

In order to assess whether MSLT results might have been influenced by poor sleep in the first recorded night, MSLT values were compared (stepwise linear regression) with indicators of sleep quality: TST, SEI, Stage 1, Stage 2, SWS, Wake Time, Movement Time and REM time. Also, as the mean Total Sleep Time was rather low for the group (330 minutes), potential association between TST and scores of fatigue and sleepiness were evaluated. These two analyses did not yield significant results.

## DISCUSSION

First, we confirm a relatively high prevalence of PSD and sleepiness in non-selected CFS patients, with 46% of them fulfilling criteria for at least one sleep disturbance and 30% presenting with objective sleepiness as measured by the MSLT. Thus, PSD and sleepiness are absent in a majority of CFS cases, and CFS cannot be reduced to either of these syndromes. Moreover, the magnitude of the PSD in this population is questionable. There is a lack of consistency in the literature concerning the optimal AHI cutoff for clinically significant respiratory events. A maximum of five respiratory episodes per hour is usually recommended, as was employed in our study. On the other hand, it is generally considered necessary to treat only those patients having an AHI greater than 20 per hour (He, 1988). Depending on the threshold used, the prevalence of sleep respiratory disturbances, and hence the total percentage of patients suffering from primary sleep disorders, varies considerably. In the first case, 45.7% of our patients (21 patients with an AHI above 5, including two patients who also presented with more than three episodes of PLM) would be defined as having a comorbid diagnosis with CFS. Using the cutoff of AHI of 20 per hour, only 10.9% of our sample would be considered to have a PSD (three patients with an AHI\\(\geq20\), plus the two patients with more than three episodes of PLM who had an AHI<20). It should also be remembered that such sleep disturbances can be found in a normal population. In a large cohort of unselected subjects (Young et al., 1993), 4.4% of women and 6.2% of men between 30 and 39 years old had an AHI superior to 15 (as compared with 5.5% of the women and 16% of the men in this group). PLMs were found in about 6% of normal medical center personnel without sleep complaints (Kales et al., 1992), a rate comparable to the 4.3% found in our sample.

Secondly, objective and subjective sleepiness were not found to be associated with PSD. This lack of relationship in the present study is in contrast to well documented positive associations (e.g., Valencia-Flores et al., 1993). The relatively low level of respiratory disorders encountered here may offer a partial explanation. Sleepiness is only present in one-third of CFS cases, and is not even associated with those CFS cases where a PSD is also present. This supports previous data (Lichstein et al., 1997) showing that sleepiness does not predict fatigue and confirms that the two symptoms should be considered separately.

Thirdly, regression analyses showed no association between PSD or objective sleepiness and any of the several dimensions of fatigue that were measured (anxiety, depression, somatisation, fatigue, functional status impairment). The presence of associated psychiatric diagnoses was not significantly different in any of the subgroups studied. Only fibromyalgia, which is frequently comorbid with CFS, was

### Table 3: Fatigue Indicators Split by PSD and MSLT

<table>
<thead>
<tr>
<th>SCORES (mean ±SD)</th>
<th>PSD+</th>
<th>PSD-</th>
<th>Significance</th>
<th>MSLT&lt;10</th>
<th>MSLT&gt;10</th>
<th>Significance</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAS</td>
<td>27.5 (6.0)</td>
<td>29.1 (6.6)</td>
<td>NS</td>
<td>25.8 (5.5)</td>
<td>29.5 (6.8)</td>
<td>NS</td>
<td>28.4 (6.6)</td>
</tr>
<tr>
<td>HDS</td>
<td>18.4 (5.9)</td>
<td>19.3 (6.2)</td>
<td>NS</td>
<td>18.3 (4.3)</td>
<td>19.3 (6.7)</td>
<td>NS</td>
<td>19.0 (6.0)</td>
</tr>
<tr>
<td>SOMGEN</td>
<td>33.0 (9.6)</td>
<td>32.6 (10.2)</td>
<td>NS</td>
<td>29.0 (9.6)</td>
<td>34.4 (9.6)</td>
<td>NS</td>
<td>32.8 (9.8)</td>
</tr>
<tr>
<td>SOMCFS</td>
<td>31.6 (11.2)</td>
<td>33.6 (9.8)</td>
<td>NS</td>
<td>28.9 (7.4)</td>
<td>33.7 (11.3)</td>
<td>NS</td>
<td>31.9 (9.7)</td>
</tr>
<tr>
<td>CIS-1</td>
<td>51.3 (6.8)</td>
<td>49.4 (9.9)</td>
<td>NS</td>
<td>48.6 (10.6)</td>
<td>51.0 (7.6)</td>
<td>NS</td>
<td>50.2 (8.6)</td>
</tr>
<tr>
<td>CIS-2</td>
<td>25.7 (8.0)</td>
<td>25.9 (7.7)</td>
<td>NS</td>
<td>25.1 (7.2)</td>
<td>26.1 (8.1)</td>
<td>NS</td>
<td>25.8 (7.8)</td>
</tr>
<tr>
<td>CIS-3</td>
<td>17.0 (6.1)</td>
<td>17.1 (6.5)</td>
<td>NS</td>
<td>15.6 (6.1)</td>
<td>17.7 (6.7)</td>
<td>NS</td>
<td>17.0 (6.4)</td>
</tr>
<tr>
<td>CIS-4</td>
<td>16.5 (5.2)</td>
<td>15.1 (5.3)</td>
<td>NS</td>
<td>17.0 (3.8)</td>
<td>15.2 (5.8)</td>
<td>NS</td>
<td>15.7 (5.3)</td>
</tr>
<tr>
<td>CIS-T</td>
<td>111.4 (19.2)</td>
<td>109.2 (22.4)</td>
<td>NS</td>
<td>108.6 (22.1)</td>
<td>110.7 (20.5)</td>
<td>NS</td>
<td>110.1 (20.8)</td>
</tr>
<tr>
<td>SIP-T</td>
<td>25.9 (8.8)</td>
<td>20.7 (15.6)</td>
<td>NS</td>
<td>26.7 (9.1)</td>
<td>21.5 (14.4)</td>
<td>NS</td>
<td>23.1 (13.1)</td>
</tr>
<tr>
<td>PATIENTS (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>psy diagnosis</td>
<td>11</td>
<td>18</td>
<td>NS</td>
<td>8</td>
<td>21</td>
<td>NS</td>
<td>29</td>
</tr>
<tr>
<td>fibromyalgia</td>
<td>11</td>
<td>11</td>
<td>NS</td>
<td>3</td>
<td>19</td>
<td>(p=0.0178)</td>
<td>22</td>
</tr>
</tbody>
</table>

PSD+/−: patients with at least one/no primary sleep disorder; MSLT<10≥10: patients with Multiple Sleep Latency Test less/more than or equal to 10 minutes; HAS: score on Hamilton anxiety scale; HDS: score on 17-item Hamilton depression rating scale; SOM-GEN: Somatisation score from SCL-90; SOMCFS: selected somatization items for CFS; CIS1-4 and T: score on the Checklist Individual Symptoms, items 1-4 and total; SIP: score on the Sickness Impact Profile, sum of items; finger tapping: number of taps; psy diagnosis: number of patients with at least one psychiatric diagnosis. Logistic regression was used in all analyses.
found to be infrequent (3 of 22) among the patients more prone to sleepiness as indicated by short MSLT (<10 minutes). The significance of this finding merits further elucidation, as this result was confirmed by an exact test and is unlikely to be due to chance alone.

Some limitations exist in this study. Sleepiness was measured only punctually (two self-rating scales and four MSLT in less than 24 hours), so that results may not represent long-term sleepiness. PLMs were recorded randomly on the left or right leg, for technical limitations. Since periodic limb movements can be unilateral (Lugaresi et al., 1965; Coleman, 1982), the prevalence of PLM might be slightly more elevated than what was observed here. However, bilateral measures of periodic limb movements are more important for quantification, while our objective was essentially screening. Another possible limitation is the tertiary care setting, where comorbid conditions may be over-represented. However, a high level of psychopathology in CFS in primary care has been demonstrated, suggesting that the association of CFS and psychopathology in tertiary referral centers does not merely reflect a more severely ill group (Euba et al., 1996). Some measurements were performed using self-rating scales, which generally lack the large extent of validation from which interview-based scales benefit. However, the acceptable to very good normal distribution in the studied sample is in favor of their value.

In summary, about 46% of patients present comorbid primary sleep disorders, this being reckoned with conservative criteria (only 11% with demanding criteria), and 30% with objective sleepiness. Although the presence of aspecific sleep alterations has been demonstrated previously in CFS, the participation of classical PSD per se seems of minimal importance, and it is difficult to reduce CFS to a somatic expression of a PSD or as a mere translation of sleepiness. In fact, both subjective and objective measures of sleepiness showed limited association with CFS, suggesting sleepiness deserves to be studied separately. This study leaves open the question of potential clusters within the chronic fatigue syndrome. Longitudinal protocols should be encouraged, as they may determine whether such clusters have a different clinical outcome.

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