Sleep and Periodic Limb Movement in Sleep in Juvenile Fibromyalgia

Catherine E. Tayag-Kier, MD*; Gregory F. Keenan, MD‡; Lisabeth V. Scalzi, MD‡; Brian Schultz, RPSGT*; Joanne Elliott, RPFT*; Huaqing Zhao, MA§; and Raanan Arens, MD*

ABSTRACT. Objectives. Fibromyalgia has been recently recognized in children and adolescents as juvenile fibromyalgia (JF). In adult fibromyalgia, subjective complaints of nonrestorative sleep and fatigue are supported by altered polysomnographic findings including a primary sleep disorder known as periodic limb movements in sleep (PLMS) in some subjects. Although poor sleep is a diagnostic criterion for JF, few reports in the literature have evaluated specific sleep disturbances. Our objectives were to evaluate in a controlled study the polysomnographic findings of children and adolescents with JF for alterations in sleep architecture as well as possible PLMS not previously noted in this age group.

Methods. Sixteen consecutive children and adolescents (15.0 ± 2.6 years of age) diagnosed with JF underwent overnight polysomnography. Polysomnography was also performed on 14 controls (14.0 ± 2.2 years of age) with no history of an underlying medical condition that could impact on sleep architecture. Respiratory variables, sleep stages, and limb movements were measured during sleep in all subjects.

Results. JF subjects differed significantly from controls in sleep architecture. JF subjects presented with prolonged sleep latency, shortened total sleep time, decreased sleep efficiency, and increased wakefulness during sleep. In addition, JF subjects exhibited excessive movement activity during sleep. Six of the JF subjects (38%) were noted to have an abnormally elevated PLMS index (>5/hour), indicating PLMS in these subjects.

Conclusion. Our study demonstrated abnormalities in sleep architecture in children with JF. We also noted PLMS in a significant number of subjects. This has not been reported previously in children with this disorder. We recommend that children who are evaluated for JF undergo polysomnography including PLMS assessment. Pediatrics 2000;106(5). URL: http://www.pediatrics.org/cgi/content/full/106/5/e70; juvenile fibromyalgia; periodic limb movement in sleep; restless legs syndrome.

ABBREVIATIONS. JF, juvenile fibromyalgia; PLMS, periodic limb movement in sleep; EEG, electroencephalogram; ECG, electrocardiogram; SpO2, oxygen saturation; PTCO2, expired end-tidal carbon dioxide tension; EMG, electromyogram; REM, rapid eye movement; SD, standard deviation; RLS, restless legs syndrome.

Fibromyalgia, a common disorder in adults, has been recently recognized in children and adolescents. Yunus and Masi proposed criteria for the diagnosis of juvenile fibromyalgia (JF). These include generalized musculoskeletal aching (3 or more sites for 3 or more months), typical tender points (5 or more of the 18 sites located at specific parts of the body), and at least 3 clinical features (of the 10 described; Table 1).

In adults with fibromyalgia, sleep-related complaints are common and include poor sleep, waking up feeling tired, excessive daytime somnolence, and chronic fatigue. These subjective complaints are supported by polysomnography findings. Excessive movements during sleep, leading at times to periodic limb movements in sleep (PLMS), have also been reported. The latter were linked to disruption of normal sleep architecture.

However, only a few reports in the literature assess sleep disturbances in JF. Yunus and Masi reported poor sleep in 67% of 33 of patients younger than 17 years of age. In a telephone interview, 96% of 45 children and adolescents followed by Siegel et al reported sleep disturbances. Based on polysomnographic data, Roizenblatt et al reported on decreased sleep efficiency, increased arousals, and disturbed electroencephalogram (EEG) frequency during slow-wave sleep in this group of children. Finally, Moldofsky et al reported on restless during sleep as indicated by the increase in movement/arousal activity in this group.

Our objectives were to assess in a controlled study the polysomnographic findings and sleep patterns in children and adolescents with JF and to search for the specific movement arousal disorder PLMS, reported previously in adults with fibromyalgia but not recognized in children.

METHODS

Study Group

We studied 16 consecutive children and adolescents (15.0 ± 2.6 years of age; 9.2–18.2 years of age) diagnosed with JF according to the clinical criteria set by Yunus and Masi (Table 1). These patients had been referred through the Rheumatology Section at Children’s Hospital of Philadelphia (Philadelphia, PA). All subjects were asked about other medical conditions, psychiatric or behavioral disorders, pregnancy, and drug abuse. In addition, sleep-related complaints were obtained from all subjects (Table 2).

Control Group

We studied 14 healthy children and adolescents (14.0 ± 2.2 years of age; 9.4–16.8 years of age), recruited from families of hospital personnel. All controls were matched by age, gender, and sexual maturation to the study group. All had a negative history...
TABLE 1. Suggested Criteria for Diagnosis of JF

<table>
<thead>
<tr>
<th>Feature</th>
<th>JF (n = 16)</th>
<th>Control (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor sleep, n (%)</td>
<td>16 (100)*</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Daytime fatigue, n (%)</td>
<td>11 (69)*</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Leg pains/restlessness before or during sleep, n (%)</td>
<td>5 (31)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Family history of PLMS/RLS, n (%)</td>
<td>0 (0)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Family history of fibromyalgia, n (%)</td>
<td>2 (12.5)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

* P < .005 versus control; ** P < .0001 versus control.

TABLE 2. Sleep-Related Complaints

<table>
<thead>
<tr>
<th>Complaint</th>
<th>JF (n = 16)</th>
<th>Control (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain in the morning</td>
<td>13 (81)*</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Pain in the morning</td>
<td>13 (81)*</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>12 (75)*</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>11 (69)*</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Daytime fatigue</td>
<td>11 (69)*</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Leg pains/restlessness</td>
<td>5 (31)</td>
<td>1 (7)</td>
</tr>
<tr>
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<td>0 (0)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Family history of fibromyalgia</td>
<td>2 (12.5)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

* P < .005 versus control; ** P < .0001 versus control.

Arousals were scored according to American Sleep Disorders Association and Sleep Research Society Task Force criteria and slightly modified for a pediatric population as suggested by others. Accordingly, an arousal was defined as an abrupt shift in EEG frequency lasting 2 or more seconds and accompanied by one or more following changes in recording signals: increased chin or EMG activity, increased heart rate, EEG distortion, and distortion of the respiratory signals (air flow, chest/abdominal effort, and P_2CO2). An arousal needed to be preceded by at least 10 continuous seconds of sleep. In addition, an arousal from REM sleep required an increase in submental EMG amplitude. The arousal index was the number of arousals per hour of sleep. An awakening was defined as an arousal lasting >15 seconds or Wake score according to the criteria of Rechtschaffen and Kales. Awakening index was the number of awakenings per hour of sleep.

Periodic limb movements in sleep were scored if they were part of a series of 4 or more consecutive leg movements lasting 5 to 5 seconds, with an intermovement interval of 5 to 90 seconds. Periodic limb movement in sleep index was the number of PLMS per hour of sleep, an index >3 was considered pathologic. In addition, we scored the number of PLMS leading to an arousal or an awakening per hour of sleep (PLMS arousal index and PLMS awake index, respectively).

Data Analysis

Numerical data were expressed as mean ± standard deviation (SD). Unpaired t test was used to compare age and polysomnography measurements between the JF subjects and controls. Fisher’s exact test was used to compare gender and sleep complaints. Kruskal-Wallis test was used to compare sexual maturation ( Tanner staging). For parameters with skewed distribution, nonparametric test was used to confirm the results. A P value of <.05 was defined as statistically significant.

RESULTS

We studied 16 consecutive JF subjects, of whom 15 were females, and 14 controls, of whom 13 were females. There were no significant differences in age (P = .29), gender (P = 1), and sexual maturation (P = .68 for breast scores and P = .46 for pubic hair scores) between the JF subjects and controls. Sleep-related complaints were more prominent in the JF subjects (Table 2).

Of the 16 JF subjects, 11 were not receiving any medications before and during polysomnography. Of the remainder, 3 patients discontinued their medications 3 days before the study as instructed (1 on each of the following: nortriptyline, imipramine, and cyclobenzaprine), and 2 patients elected to continue their medications (1 on paroxetine, 1 on amitriptyline).

Subjects with JF did not show evidence of sleep-disordered breathing. Their oxygenation and ventilation were normal and similar to controls (Table 3). However, JF subjects differed significantly from controls in sleep architecture (Table 4). JF subjects presented with difficulties initiating sleep as evident by prolonged sleep latency. They had shortened total...
sleep time and decreased sleep efficiency related to increased wakefulness during sleep. Sleep stages (1–4 and REM) as percent of sleep period time were similar to controls except that they spent twice the time awake. We noted α-δ sleep in 1 JF subject. Arousal and awakenings indices were similar to the control group.

We noted that JF subjects exhibited excessive movements during sleep and in particular were noted to have significantly more PLMS resulting in higher PLMS indices (Table 5). Arousals and awakenings secondary to PLMS were also significantly higher in subjects with JF. Abnormally elevated PLMS indices >5/hour were noted in 6 subjects (38%). None were on, or withdrew from, tricyclic antidepressants during this period. However, 1 subject was on paroxetine. The JF subjects with PLMS did not differ in their clinical presentation compared to the control group.

We report abnormal sleep patterns in JF subjects. Based on overnight polysomnography, we noted significant alterations in sleep architecture that include shortened total sleep time, prolonged sleep latency, decreased sleep efficiency, and longer awake periods during sleep. In addition, we noted in a significant number of subjects the presence of a movement arousal disorder of PLMS not reported previously in JF.

Sleep-related complaints are commonly reported in adults with fibromyalgia.4–6 Similar complaints of nonrestorative sleep have recently been recognized as part of the manifestation of JF.1–3 Still unclear are the mechanisms altering sleep in this disorder. There is growing evidence that factors altering initiation of sleep as well as the existence of a movement arousal disorder are part of the clinical spectrum of fibromyalgia.7 Any of the above may alter normal sleep architecture and significantly impact on daily activity, performance, pain threshold, and psychological profile of these subjects.

We found no evidence of sleep-disordered breathing in JF, although respiratory abnormalities have been previously reported in adults with fibromyalgia.4 Obstructive sleep apnea should be excluded in any polysomnographic assessment of JF, because it has also been shown to be associated with excessive motor activity during sleep in children.14

Our polysomnographic data confirm the finding of decreased sleep efficiency reported by Roizenblatt et al.3 However, sleep efficiency could be reduced by several factors such as prolonged sleep latency, reduced total sleep time, and increased wakefulness periods during sleep. We found alterations in all of these domains in our study. α-δ sleep is an EEG pattern of α intrusion into non-REM sleep. Although this has been described in some adults with fibromyalgia and was associated with nonrestorative sleep,7,5,8 only one of the JF subjects showed evidence of this phenomenon.

The reason for prolonged sleep latency or insomnia in our subjects is not clear. As mentioned above, JF subjects entered a consolidated sleep stage only after 43 ± 55 minutes in comparison to 8 ± 6 minutes (P < .05) in the control group. Insomnia should be first considered in the context of anxiety/depressive disorders, both reported to exist in high prevalence in adults with fibromyalgia4 as well as in JF.1,2,18 Second, insomnia has been associated in adults with fibromyalgia with excessive limb restlessness just before sleep.19 This phenomenon, known as restless legs syndrome (RLS), is characterized by unpleasant leg sensations and is relieved by voluntary movement of the lower limbs.20

Five of our JF subjects reported leg pains/restlessness before or during sleep that were associated with an unpleasant sensation. In all of these subjects, we noted excessive leg EMG activity before sleep and at times of wakefulness during sleep. Although, the criteria for RLS have been suggested in children,21 we were cautious of diagnosing RLS in these subjects because there is no consensus yet for this diagnosis in children.

Polysomnographic findings in our study showed that a subset of JF subjects had a primary sleep disorder known as PLMS. Six of 16 subjects (38%)
showed a significantly higher PLMS index. The subset of JF subjects with PLMS could not be differentiated from the JF subjects without PLMS based on clinical presentation alone. For all JF subjects the PLMS index was found to be ninefold higher than for the controls. Previous studies in children evaluating PLMS used criteria for diagnosis based on adult literature indicating PLMS index >5/hour as pathologic.22–24 Although we used the above criteria, our data derived from the controls are very similar suggesting a PLMS index above of 3.6/hour (mean ± 2 SD) as the upper limit of normal among children and adolescents.

In our study, the number of arousals and awakenings in JF subjects was similar to controls. However, arousals and awakenings secondary to PLMS were significantly higher in this group. As mentioned, wakefulness after sleep onset was significantly higher in JF subjects. Therefore, we speculate that PLMS induces longer awakenings in JF.

Periodic limb movement in sleep, originally called nocturnal myoclonus, typically occurs in the middle and older ages and has previously been observed in adults with fibromyalgia7,8 but not in JF. PLMS is associated with various medical conditions such as: myelopathies, neuropathies, diabetes mellitus, uremia, decreased iron stores, as well as familial clustering. Tricyclic antidepressants may induce PLMS25,26 as does withdrawal from a variety of medications, such as anticonvulsants, benzodiazepines, and barbiturates.27 This is especially relevant to patients with fibromyalgia who often receive tricyclic antidepressants. In our study, none of the subjects diagnosed with PLMS received or withdrew from tricyclic antidepressant during the study. One subject diagnosed with PLMS continued with paroxetine; however, this medication has not been reported to induce PLMS.

Despite the fact that the neurophysiological mechanism leading to PLMS is unknown,7 PLMS is considered a central nervous system dysfunction and frequently responds to pharmacological modalities.28,29 The present study shows that polysomnography is a useful tool to detect abnormalities in sleep architecture and the presence of PLMS in children and adolescents diagnosed with JF. Polysomnography can provide additional objective evidence to the present clinical criteria for diagnosis of JF and sleep-related complaints.

CONCLUSION

Our study demonstrated abnormalities in sleep architecture in children with JF. We also noted a movement disorder in sleep known as PLMS to occur in a significant number of subjects and not reported previously in children with this disorder. We recommend that children who are evaluated for JF undergo polysomnography, including PLMS assessment, as part of this evaluation.

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Pediatrics 2000;106;e70
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