Exploring the Relationship Between Fatigue and Sleep Disturbances in Multiple Sclerosis

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ABSTRACT

Rationale and Background: The pathophysiology of fatigue in Multiple Sclerosis (MS) remains unclear and sleep disturbances were suggested to be a contributing factor. This study therefore aimed to evaluate the relationship between fatigue and sleep disturbances in MS.

Patients and Methods: We included 20 MS patients in the age range of 20-40 years old, 10 patients with fatigue and 10 patients without fatigue, and 10 control subjects. All patients were subjected to the detailed neurological evaluation, Expanded Disability Status Scale (EDSS), Fatigue Severity Scale (FSS), Beck's Depression Inventory (BDI) and Epworth Sleepiness Scale (ESS). Patients and controls underwent whole night polysomnography (PSG).

Results: The MS patients had an increased number of awakenings, longer sleep latency and less sleep efficiency and slow wave sleep compared to the controls. Only one patient in the fatigued group had an increased periodic limb movement index while two patients in the non-fatigued group had an increased apnea hypopnea index due to obstructive events. We found a significant positive correlation between sleep latency and BDI score (P=0.037) and FSS score (p= 0.04).

Conclusion: We found that sleep disturbances do not seem to be a major contributing factor to fatigue in MS. Although the MS patients had less sleep efficiency and slow wave sleep and longer sleep latency than the control subjects, there was not a difference in the different sleep variables between the fatigued and non-fatigued patients. (Egypt J. Neurol. Psychiat. Neurosurg., 2009, 46(1): 193-202)

INTRODUCTION

Fatigue is the most frequent symptom in multiple sclerosis (MS). It is reported by 76% to 92% of patients¹,². It is defined according to the MS Council³ as "the subjective lack of physical and/or mental energy that is perceived by the individual or the caregiver to interfere with usual or desired activities". More than 55% of patients report it as the worst symptom⁴. It affects employment and limits social relationships and self care activities⁵,⁶. It also affects cognitive functions in the form of impairing thought process and the ability to cope and concentrate⁷. Furthermore, it may precipitate irritability, anxiety and depression⁸. The mechanism underlying development of fatigue in MS remains unclear. Although fatigue is believed to be a primary symptom of MS related to the demyelinating process of the disease, fatigue may be secondary to other factors such as sleep disturbances, depression and medication effect⁹. Approximately half of all patients with MS report sleep-related problems⁹.

The most common sleep disorders seen in patients with MS insomnia, nocturnal movement disorders, sleep-disordered breathing, narcolepsy, and rapid eye movement sleep behavior disorder. Important consequences of disrupted sleep are daytime somnolence and increased fatigue¹⁰. Awareness and treatment of these conditions is vital to improving the health and quality of life in patients with MS.

The aim of this study is to explore the relationship between fatigue and sleep disturbances in MS. The hypothesis that fatigue in MS is caused, even partially, by sleep disturbances will be elucidated. Furthermore characterization of sleep disturbances in MS, if present, will be discussed.
PATIENTS AND METHODS

Patients
This study was conducted on 20 patients diagnosed with MS according to Mc Donald' criteria, had relapsing remitting or secondary progressive MS. The patients were divided into two groups according to the fatigue severity scale (FSS); group (1) Ten patients with fatigue and group (2) 10 patients without fatigue. We included patients in the age range of 20-40 years old. Patients had history of drug intake that may affect sleep such as hypnotics and sedatives, patients in acute exacerbation to rule out role of cytokines in fatigue, patients had primary progressive type of MS and patients on Interferon therapy as it may cause fatigue were excluded from this study. Control group of 10 healthy age and sex matched individuals had no complaints of fatigue or sleep disorders and not receiving any medication that may affect sleep.

Methods
Our participants underwent the following battery of evaluation:

A) Clinical assessment including full history taking and a general medical and neurological examination. The following scales were completed:

* Expanded disability status scale (EDSS):
EDSS quantifies disability in MS patients in eight functional systems; pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral and other systems. EDSS steps 1.0 to 4.5 refer to people who are fully ambulatory, EDSS steps 5.0 to 9.5 refer to impairment of ambulation.

* Fatigue evaluation using fatigue severity scale (FSS):
FSS is a nine–item standardized questionnaire assessing functional and behavioral aspects of fatigue. The FSS has a possible score range of 1 to 7. Patients were considered to be fatigued if FSS score was at least five.

* Sleep evaluation using Epworth sleepiness scale (ESS):
ESS is a questionnaire that assesses subjective sleepiness and relies on dosing behavior in eight different situations. It asks the patient to rate the likelihood of falling asleep on a scale from 0 to 3, where 0 indicates no chance of dosing and 3 indicates the greatest chance of dosing. A score of at least 10 is indicative of excessive daytime sleepiness.

* Evaluation of depression using Beck's depression scale (BDI):
The BDI is a 21 item questionnaire which assesses dysphoria, anhedonia, suicidal ideation and cognition-related symptoms on a three-point scale. Scores on the BDI range from 1 to 40, a score of at least 11 is a cut off point for normality, and a score of 16 is indicative of major depression.

* Body mass index (BMI):
BMI provides a simple and the most useful measure of obesity in adults, which is body weight (kg) divided by height squared (m2). A BMI of 30 kg/m2 is widely recognized as a cut-off point for obesity.

B) Neuroradiological Assessment:
Magnetic resonance imaging (MRI) of the brain & cervicodorsal spinal cord was performed recording T1, T2 weight axial images and FLAIR axial images. In addition to diagnosing MS according to Mc Donald' criteria, we aimed to identify lesion load (total, supratentorial, infratentorial and spinal cord lesion load) using MRI.

C) Polysomnography (PSG):
A full night polysomnography recording was carried out using an Embla amplifier and Somnologica software. During the PSG the following electrophysiological data were recorded: electroencephalography, electrooculogram, submental and bilateral anterior tibial electromyogram,
respiratory effort, airflow, EKG, snoring, oxygen saturation and body position.

The polysomnography was scored according to the standardized Rechtschaffen and Kales\textsuperscript{18} criteria by an experienced sleep disorder physician who was blinded to the diagnosis and treatment of our subjects.

**Statistical analysis**

Statistical package for social science (SPSS) was used for data management and analysis. The Mann-Whitney test was used for comparison of qualitative variables, while Spearman's test was used for correlations.

## RESULTS

### A) Clinical data:

The age of the MS patients with fatigue ranged from 20 – 40 years with a mean of 27.7±6.52. The age of the MS patients without fatigue ranged from 20- 40 with a mean of 28.8± 6.65. The age of the controls ranged from 20- 40 with a mean of 26.3±7.07. There was no significant difference in age between the groups. There was also no difference in the sex distribution between the groups. Also duration of the illness did not differ between the group of the MS patients with fatigue (5.5±3.62) and the MS patients without fatigue (4.8±2.62). Moreover, there was no difference between the two group as regards the type of MS (RR or SP) (P value = 0.14).

Comparison of the scores of EDSS, BDI and ESS between the fatigued and non-fatigued patients showed no statistically significant difference (Table 1).

### B) Radiological Data:

Comparison of the radiological data including the total MRI load, the supratentorial load, the infratentorial load and the spinal cord load between the fatigued and non-fatigued patients did not show a significant difference (Table 2).

### C) Polysomnographic Data:

We did not find any difference in PSG between the MS patients complaining of fatigue and those without fatigue complaint as shown in table (3).

We found two subjects in the non-fatigued group who had an Apnea Hypopnea Index (AHI) more than 5/hour, while there was not any patient in the fatigued group had a high index more than 5/hour. The events noted were mainly obstructive. Also we found only one patient in the fatigued group who had a high periodic limb movements (PLM) index (11.7/hour) while none in the non-fatigued group had an index more than 5/hour.

Comparison of polysomnographic data between the MS patients and the control group showed that the sleep efficiency was significantly less in the MS patients than the control group (p=0.001). Moreover, the number of awakenings was higher in the patients than the controls (p>0.001). Also the sleep latency was longer in the MS patients compared to the control group (p=0.02). The percentage of slow wave sleep was much less in the MS patients than the controls (p>0.001). Otherwise, there was no significant difference in the other PSG parameters between the MS patients and the controls (Table 4).

**Correlation Between the Clinical Data, MRI Load and Sleep Parameters in MS Patients**

- A significant positive correlation between sleep latency and BDI score (r=0.409, P=0.037) and FSS score (r=0.391, p=0.04) (Fig. 1).
- A significant positive correlation between BDI score and total MRI load (r=0.43, P=0.029).
- No other significant correlation was found between the other parameters.

### Table 4. Comparison of the clinical scores between patients groups.

<table>
<thead>
<tr>
<th>Scores</th>
<th>Group (1) Fatigued patients</th>
<th>Group (2) Non fatigued patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>EDSS</td>
<td>4.25</td>
<td>1.62</td>
<td>3.16</td>
</tr>
<tr>
<td>BDI</td>
<td>17.8</td>
<td>10.53</td>
<td>14.1</td>
</tr>
<tr>
<td>ESS</td>
<td>7.2</td>
<td>3.99</td>
<td>5.3</td>
</tr>
</tbody>
</table>
(EDSS) Expanded disability status scale, (BDI) Beck’s depression scale, (ESS) Sleep evaluation using Epworth sleepiness scale.

Table 2. Comparison of radiological data between patients groups.

<table>
<thead>
<tr>
<th>Radiological data</th>
<th>Group (1) Fatigued patients</th>
<th>Group (2) Non Fatigued patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Total MRI load</td>
<td>11.1</td>
<td>1.85</td>
<td>10.5</td>
</tr>
<tr>
<td>Supratentorial load</td>
<td>8.1</td>
<td>1.79</td>
<td>8.7</td>
</tr>
<tr>
<td>Infratentorial load</td>
<td>1.7</td>
<td>1.57</td>
<td>1.2</td>
</tr>
<tr>
<td>Spinal load</td>
<td>1.5</td>
<td>2.07</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Table 3. Comparison of Polysomnographic data between patients groups.

<table>
<thead>
<tr>
<th>Polysomnographic Data</th>
<th>Group (1) Fatigued patients</th>
<th>Group (2) Non Fatigued patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>TST (min)</td>
<td>300.14</td>
<td>79.8</td>
<td>311.45</td>
</tr>
<tr>
<td>Number of awakenings</td>
<td>13.9</td>
<td>4.1</td>
<td>13.1</td>
</tr>
<tr>
<td>Arousal index</td>
<td>16.5</td>
<td>8.7</td>
<td>10.9</td>
</tr>
<tr>
<td>Sleep latency(min)</td>
<td>66.74</td>
<td>71.75</td>
<td>37.03</td>
</tr>
<tr>
<td>REM latency</td>
<td>120.1</td>
<td>74.25</td>
<td>173</td>
</tr>
<tr>
<td>Stage I%</td>
<td>9.12</td>
<td>4.11</td>
<td>10.98</td>
</tr>
<tr>
<td>Stage II%</td>
<td>57.97</td>
<td>15.37</td>
<td>50.39</td>
</tr>
<tr>
<td>SWS%</td>
<td>20.26</td>
<td>11.71</td>
<td>24.33</td>
</tr>
<tr>
<td>REM %</td>
<td>15.67</td>
<td>9.45</td>
<td>14.28</td>
</tr>
<tr>
<td>Sleep efficiency %</td>
<td>76.03</td>
<td>15.63</td>
<td>71.87</td>
</tr>
</tbody>
</table>

TST= total sleep time, REM= rapid eye movement, SWS= slow wave sleep.

Table 4. Comparison of Polysomnographic data between the MS patients and controls.

<table>
<thead>
<tr>
<th>Polysomnographic data</th>
<th>Patients</th>
<th>Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>TST (min)</td>
<td>305.8</td>
<td>74.2</td>
<td>390.4</td>
</tr>
<tr>
<td>No of awakening</td>
<td>12.4</td>
<td>6.9</td>
<td>3.7</td>
</tr>
<tr>
<td>Sleep latency(min)</td>
<td>51.9</td>
<td>57.9</td>
<td>12.7</td>
</tr>
<tr>
<td>REM latency</td>
<td>146.6</td>
<td>97.1</td>
<td>153.7</td>
</tr>
<tr>
<td>Stage I%</td>
<td>10.1</td>
<td>5.6</td>
<td>11.4</td>
</tr>
<tr>
<td>Stage II%</td>
<td>54.2</td>
<td>13.6</td>
<td>48.3</td>
</tr>
<tr>
<td>SWS%</td>
<td>14.8</td>
<td>10.7</td>
<td>31.1</td>
</tr>
<tr>
<td>REM %</td>
<td>14.9</td>
<td>9.1</td>
<td>10.4</td>
</tr>
</tbody>
</table>
**DISCUSSION**

The aim of the present work was to evaluate sleep in MS patients with fatigue, both subjectively and objectively, and to find if there is a relation between fatigue and sleep disturbances in MS.

There was not a significant difference in age between the MS patients with fatigue and those without fatigue. Previous studies did not report any age difference between fatigued and non-fatigued MS patients or any correlation between fatigue in MS and age, which is in concordance with our results\(^{19,20}\). Conversely Yet Colosimo et al.\(^{21}\) found that elder patients had a significantly higher risk of fatigue. Perhaps age has a selective effect on fatigue induced by different types of MS, as suggested by a positive correlation between age and fatigue in primary progressive (PP) type of MS only and not in relapsing remitting (RR) or secondary progressive (SP) types\(^{22}\). In agreement with our results, previous studies had found that there is no difference between men and women with MS in their perception of fatigue\(^{19,21,22,23}\).

<table>
<thead>
<tr>
<th>Sleep efficiency %</th>
<th>73.9</th>
<th>15.2</th>
<th>89.3</th>
<th>3.7</th>
<th>0.001</th>
</tr>
</thead>
</table>

TST= total sleep time, REM= rapid eye movement, SWS= slow wave sleep.

Fig. (1): Correlation between FSS score and sleep latency.
We found no difference in disease duration between the fatigued and non-fatigued group. Furthermore there was no correlation between the FSS and duration of illness. This is in agreement with previous studies. However, this is contradicted by the results of Lerdal et al., who found that FSS score in MS patients showed a positive correlation with time since disease onset.

In the present study, in agreement with Bakshi et al., there was no significant difference in MS disease types, whether relapsing-remitting (RR) or secondary progressive (SP) MS, between the fatigued and non-fatigued patients. Although some studies found that progressive MS patients had higher fatigue scores than RR MS patients, Kroencke et al. stated that an analysis of covariance revealed that this apparent difference in their patients was in fact attributable almost exclusively to differences in disability among the subtypes of MS rather than to the subtype itself.

In present study, there was no relation between neurological disability and fatigue as there was no difference in EDSS score between the fatigued and non-fatigued group. This is supported by previous studies. On the other hand, this is contradicted by other researchers who reported a positive correlation between EDSS and fatigue. It is possible that fatigue is influenced by certain specific items in the EDSS scale as it was reported that fatigue was associated with the occurrence of cerebellar, sphincteric, pyramidal and sensory signs, but not with brain stem, visual and cognitive impairment when the single items of EDSS were considered.

Thus we can see that research did not reach consensus about the association of fatigue with clinical or demographic variables, such as age, gender, disability, type of MS, and disease duration, a conclusion that was also reached by a previous review on fatigue in MS.

The present study did not show a statistically significant difference in depression between the two groups of MS patients. Similarly Krupp et al. found that fatigue was unrelated to depression. However, in other studies, fatigue and depression were positively correlated. Inventory, found that fatigue was strongly associated with clinically significant depressive symptoms. It was suggested that common mechanisms play a role in MS fatigue and depression including psychological factors or brain lesions in specific neuroanatomic pathways. The conflicting results on the relation between fatigue and depression may be related to the small sample size in some studies and the different scales used to assess depression in the including the Center for Epidemiologic Studies Depression Scale (CES-D), the Zung Depression Scale, Hamilton depression scale and Beck's Depression various reports.

The present study showed that ESS was similar in the fatigued and non-fatigued group. Our study revealed that the Also there was no difference in the EDSS, BDI or CES scales. Furthermore, ESS did not correlate with the FSS. Other studies have found that the MSLT, which is considered the subjective measure of sleepiness, showed normal sleep onset latency in fatigued MS patients. It is important to note that several studies have suggested that fatigue and sleepiness can be independent consequences of sleep disorders. They reported that fatigue and sleepiness are two dimensions with only limited overlap in patients with sleep disturbances and in those with MS. This was shown by absence of correlation between ESS and FSS in patients with sleep disorders, while in MS single-item analysis showed that only a subset of ESS items are significantly correlated with fatigue, as measured by the FSS. On the other hand, Attrian et al. found that using the ESS, MS patients with fatigue had an ESS score more than 10 much more often than MS patients without fatigue. However we note that in their study, the mean age of patients with fatigue was 46.4 years while the non-fatigued group had a mean age of 33.5 years. It is possible that this age difference confounded their results.

In this study in accordance to Kanyak et al., the PSG did not reveal any difference between the fatigued and non-fatigued MS patients. All the measured sleep parameters were similar in both groups. In another study, No abnormality was found in the PSG or the MSLT except an increase in the PLMI in 2 patients. The authors concluded that non-restorative sleep is unlikely mechanisms of chronic fatigue in the MS patients. So both the micro and macrostructure of sleep are not affected by fatigue and do not seem to cause it.

There was one patient in the fatigued group had a high periodic limb movement index of 11.7 per hour. However, conclusions cannot be drawn on the basis of one patient only. Kanyak et al. found that...
PLM arousal index was similar in both the fatigued and non-fatigued patients. We also found two patients in the non-fatigued group who showed an increased AHI, while none in the fatigued group had an increase AHI. Thus sleep disordered breathing does not seem to be an etiologic factor of fatigue in MS. None of our MS patients had RLS or REM sleep related behavior disorders. We found a positive correlation between FSS and sleep onset latency. We are suggesting two possible explanations for this finding. First, it is possible that there was delayed sleep phase syndrome (DSPS) in the MS patients causing increased sleep onset latency and daytime fatigue. Yet Attarian et al.\textsuperscript{35} reported that a relationship was found between fatigue and abnormal sleep cycles with DSPS being found in the fatigued group only. A detailed sleep questionnaire or actigraphy were not part of this study, thus delayed sleep phase syndrome cannot be excluded. A second possible explanation for the relation between fatigue and sleep onset latency is the presence of an organic disorder such pain or leg spasms that leads to both fatigue and increased sleep latency. Generally, patients who experience high levels of pain tend to report less sleep time, more delayed sleep onset, and increased nighttime awakenings, which in turn can further increase pain intensity and sleep disturbances\textsuperscript{35}. Using clinical evaluation, Tachibana et al.\textsuperscript{8} stated that MS patients commonly complained of difficulty initiating sleep which was attributed to spasms or discomfort in the legs. Therefore we can assume that an unrecognized organic disorder such as pain or discomfort may be responsible for causing both fatigue and sleep onset insomnia.

A positive correlation between sleep latency and BDI score was found in our study. It is stated that increased sleep onset latency is a PSG finding in depression according to the International Classification of Sleep Disorders.\textsuperscript{38} The mean BDI score of our MS patients was 15.95, while a BDI score of at least 11 is a cut off point for normality, and a score of 16 is indicative of major depression\textsuperscript{36}. Thus our patients were clearly depressed and this explains the relation between the sleep latency and the BDI score.

To evaluate the impact of MS on sleep, we compared the PSG variables between the MS patients, including both fatigued and non-fatigued groups, and the control subjects. The present study showed that the MS patients had an increased number of awakenings, decreased total sleep time and sleep efficiency compared to the controls. Several previous studies reported that MS patients had significantly lower sleep efficiency and more awakenings compared to controls suggesting that MS leads to poor sleep quality without refreshing sleep\textsuperscript{36,39}. Difficulty initiating or maintaining sleep with frequent awakenings were common complaints by MS patients\textsuperscript{38,40}. We found an increased sleep onset latency in MS patients which is subjectively interpreted as difficulty initiating sleep. As mentioned above, this finding may be caused by depression, pain and discomfort or delayed sleep phase syndrome. Naturally, a shift towards decreased sleep efficiency and increased awakenings will lead to decreased slow wave sleep in MS patients which was found in our results.

Only one of our MS patients had an increased PLMI. This does not point to an increased incidence of PLMs in MS patients. However other studies have reported a higher incidence of PLM in MS\textsuperscript{36,39}. As few studies have utilized PSG in MS patients, more data are needed on the effect of MS on PLMs. The AHI index was increased in two MS patients. This incidence of increased AHI (10\%) is not different from that reported in the general population. Young et al.\textsuperscript{34} found a prevalence of Obstructive sleep apnea syndrome (OSAS) of 24\% in males and 9\% in females when they used a threshold value of AHI of 5, which is the threshold we used in our study. Two studies utilizing PSG in MS did not find an increased AHI index in MS patients\textsuperscript{32,36}, while one study found central sleep apnea in 2 subjects out of 25 MS patients.\textsuperscript{42}

**Conclusion and recommendations**

Fatigue in MS is related to a longer sleep latency. Absence of a PSG difference between the fatigued and non fatigued groups suggests that the presence of fatigue is not related to any specific sleep disorder in MS patients. But these results must be interpreted cautiously due to small number of the patients. To the best of our knowledge, very few studies have utilized PSG in studying sleep in MS patients, thus future studies on fatigue in MS should utilize PSG preferably with additional techniques such as functional neuroimaging, actigraphy or...
inflammatory neuromediators assessment is recommended. Last, increasing the number of subjects will surely yield more powerful results.

REFERENCES

الملخص العربي

استكشاف العلاقة بين الوهن واضطرابات النوم في مرضى التصلب المتعدد

بعد عرض الوهن أكثر الأعراض شيعه عند مرضى التصلب المتعدد حيث نشير الإحصائيات إلى أن 76-92% من مرضى التصلب المتعدد يعانون من هذا العرض، ويفصل كثير من هؤلاء المرضى أن هذا العرض بعد عرض من أكثر الأعراض تأثيراً على نشاطهم اليومي وقد استهدفت هذه الدراسة تقييم نمط النوم عند المرضى المصابين بمرض الوهن وممارسته بمجرد النوم عند المرضى الذين لا يعانون من هذا العرض ومقارنة نمط النوم عند مرضى التصلب المتعدد بالأصحاء البالغين.

اشتتملت الدراسة على 20 مريضاً مصابين بمرض التصلب المتعدد 10 مريضاً يعانون من مرض الوهن و10 أخرون لا يعانون من مرض الوهن و10 من الأصحاء البالغين.

وقد تم قياس الحالات تقييماً إكلينيكياً عن طريق أخذ التاريخ المرضي والفحص الإكلينيكي تقييم درجة الإعاقة باستخدام EDSS مقياس تعقب درجة الوهن باستخدام مقياس شدة الوهن. تقييم النوم المفرط أثناء النهار باستخدام مقياس أبورث للنوم.

تقييم الإكتئاب باستخدام مقياس بيك للاكتئاب الأشعة التشخيصية للجهاز العصبي وذلك بعمل البنين المغناطيسي للمخ وتقنيات نوم باستخدام معمل النوم المتعدد. وقدي أظهرت النتائج ما يلي:

لا يوجد فرق ذو دلاله إحصائي بين المرضى الذين يعانون من الوهن والذين لا يعانون من عرض الوهن بالنسبة للنس و الجنس.

وتوزو المنصب المتناوب ودرجة الإعاقة والاكتئاب أو النوم المفرط أثناء النوم، كما لا يوجد فرق ذو دلاله إحصائي في تقييم نمط النوم بين المرضى الذين يعانون من الوهن والذين لا يعانون من الوهن.

وتوزع المنصب المتناوب ودرجة الإعاقة والاكتئاب أو النوم المفرط أثناء النوم، كما لا يوجد فرق ذو دلاله إحصائي في تقييم ال mappings بين مرضي التصلب المتعدد والأصحاء البالغين.

وقد أظهرت نتائج الأشعة التشخيصية وجود علاقة طرديه موجبة ذات دلاله إحصائي بين حجم الأصابات والذين. ولكن لا يوجد علاقة بين حجم الإصابات و شدة الوهن.

كما وجود علاقة طردية موجبة بين فترة النوم المكون و كل من شدة الوهن و درجة الاكتئاب. كانت فترة النوم المكون وعدد مرات الاستيقاظ على فرق ذو دلاله إحصائي بين مرضى التصلب المتناوبة والمريضي البالغين بينما كانت فترة النوم المعيق وكفاءة النوم أقل فرق ذو دلاله إحصائي عند مرضى الوهن مقارنة بالأصحاء.

مجموعة المرضى الذين يعانون من الوهن قد اشتملت على مرضى واحد وأنبعاث من حركات القدم الدورية اللافردية بينما اشتملت مجموعة المرضى الذين لا يعانون من أعراض الوهن على مرضى يعانون من توقف التنفس الاصطناعي أثناء النوم. وهما سيق نتختص أن اضطرابات النوم في مرضى التصلب المتناوبة ليست عاملة رئيسية في حدوث الوهن. بما أن هناك علاقة طردية موجبة بين فترة النوم المكون و شدة الوهن ربما يرجع وجود الوهن في هؤلاء المرضى إلى أسباب أخرى تؤدي إلى زيادة فترة النوم المكون مثل الالام الجسدية أو مرض تأخر فترة النوم مما يستوجب زيادة الأبحاث في هذا الموضوع.