

Fatigue and its association with sleep disorders, depressive symptoms and anxiety in patients with multiple sclerosis

Związek zmęczenia z zaburzeniami snu, objawami depresyjnymi i lękowymi u chorych na stwardnienie rozsiane

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Abstract

Background and purpose: The aetiopathogenesis of fatigue in multiple sclerosis (MS) is not clear. It could be associated with structural changes of the central nervous system, but also with mood and sleep disorders. The purpose of the study was to evaluate frequency of fatigue and its association with sleep and mood disorders in MS patients.

Material and methods: The examined group consisted of 122 MS patients (mean age 37.7 ± 10.8 years). The following questionnaires were used: Fatigue Severity Scale (FSS), Epworth Sleepiness Scale (ESS), Athens Insomnia Scale (AIS), Montgomery-Asberg Depression Rating Scale (MADRS), and Hospital Anxiety and Depression Scale (HADS).

Results: Fatigue was present in 75 MS patients (61.5%). Excessive daytime sleepiness was observed in 25 (20.5%), insomnia in 73 patients (59.8%). According to MADRS, depressive symptoms were present in 33 (27%), according to HADS in 15 people (12.3%). Anxiety was present in 32 patients (26.2%). We observed an association between fatigue (FSS) and sleep disorders (ESS, AIS) and also between fatigue and either depression (MADRS, HADS-D) or anxiety (HADS-A). The FSS score was not associated with age, sex, disease course and duration, Expanded Disability Status

Streszczenie

Wstęp i cel pracy: Etiopatogeneza zmęczenia w stwardnieniu rozsianym (SR) jest niejasna. Może mieć związek ze zmianami strukturalnymi w obrębie ośrodkowego układu nerwowego, jak również z zaburzeniami snu i nastroju. Celem pracy była ocena częstości występowania zmęczenia u chorych na SR oraz analiza zależności ze współwystępującymi zaburzeniami snu i nastroju.

Materiał i metody: W badaniu wzięło udział 122 chorych na SR (średnia wieku: $37,7 \pm 10,8$ roku). Badanie przeprowadzono za pomocą następujących kwestionariuszy: Skali Stopnia Zmęczenia (*Fatigue Severity Scale* – FSS), Skali Senności Epworth (*Epworth Sleepiness Scale* – ESS), Ateńskiej Skali Bezsenności (*Athens Insomnia Scale* – AIS), Skali Depresji Montgomery-Asberg (*Montgomery-Asberg Depression Rating Scale* – MADRS) oraz Skali Lęku i Depresji wg Zigmunda i Snaitha (*Hospital Anxiety and Depression Scale* – HADS).

Wyniki: Zmęczenie stwierdzono u 75 chorych na SR (61,5%). U 25 osób (20,5%) rozpoznano nadmierną senność w ciągu dnia, u 73 osób (59,8%) bezsenność. Według MADRS, objawy depresyjne występowały u 33 (27%), wg HADS u 15 (12,3%) osób. Objawy lękowe były obecne u 32 chorych (26,2%). Zaobserwowano korelację pomiędzy występowaniem zmęczenia (FSS) a zaburzeniami snu (ESS, AIS), objawami

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Stage (EDSS), treatment or level of education in MS patients. In inactive professionally people we noted significantly higher FSS scores (44.8 ± 13.8) in comparison with active individuals (37.2 ± 14.9 ; $p = 0.0053$).

Conclusions: Fatigue is a very common symptom in MS, sometimes associated with sleep disorders, depressive symptoms or anxiety. The treatable causes of fatigue in MS such as sleep and mood disturbances should be identified and treated.

Key words: multiple sclerosis, fatigue, depression, anxiety, sleep disorders.

Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system that affects approximately 2.5 million people around the world [1,2]. The course of the disease may vary among individuals leading to different stages of disability. One of the most common MS symptoms is fatigue, often defined as a lack of energy, tiredness, sense of exhaustion, and general weakness [2-4]. It has been reported in 40-90% of MS patients [5-8]. Fatigue significantly impairs the quality of life, and causes great socioeconomic consequences such as frequent absence from work and subsequently the loss of employment. It also interferes with daily living activities of MS patients including private life [9-13].

Despite numerous studies and extensive research, the nature and cause of fatigue in MS are poorly understood. It could be associated with structural – demyelinating – changes of the central nervous system, but also with mood and sleep disorders, which are more frequent among MS individuals than in the general population [5,14-17].

The most common sleep disturbances among MS patients include restless leg syndrome, periodic limb movement disorder, insomnia, circadian rhythm disorders, narcolepsy, and sleep-disordered breathing [18,19]. All of them may lead to excessive daytime sleepiness which sometimes could not be distinguished from fatigue. Consequently, fatigue could be a symptom of sleep disturbances [2,7,20-24].

Also depression and anxiety may accompany MS, with prevalence up to 50% [25,26]. Symptoms of depression such as the loss of motivation or anhedonia could be mistaken for fatigue, and fatigue is one of the symptoms of depression itself [3,17,27].

depresyjnymi (MADRS, HADS-D) i lękowymi (HADS-A). Nie stwierdzono zależności pomiędzy wynikiem FSS a wiekiem, płcią, przebiegiem i czasem trwania choroby, EDSS, sposobem leczenia ani poziomem wykształcenia. Osoby nieaktywne zawodowo uzyskały znamienne wyższy wynik w kwestionariuszu FSS ($44,8 \pm 13,8$) w porównaniu z osobami pracującymi zawodowo ($37,2 \pm 14,9$; $p = 0,0053$).

Wnioski: Zmęczenie jest częstym objawem występującym u chorych na SR, może towarzyszyć zaburzeniom snu, objawom depresyjnym i lękowym. Przyczyny zmęczenia poddające się terapii (zaburzenia snu i nastroju) powinny być rozpoznane i leczone.

Słowa kluczowe: stwardnienie rozsiane, zmęczenie, depresja, lęk, zaburzenia snu.

Nevertheless, some causes of fatigue in MS may be treatable (e.g. depression, anxiety or sleep disorders) and it is a challenge to find them and distinguish among individuals.

Because the link between fatigue, sleep and mood disorders is not clear in MS, the purpose of the study was to evaluate frequency of fatigue and its association with sleep disorders, anxiety and depression in MS patients – inhabitants of Silesia.

Material and methods

The examined group was recruited from 188 Silesian patients with MS treated in the Neurological Polyclinic of the Department and Clinic of Neurology in Zabrze. Of these, 122 (64.9%) agreed to take part in the study and gave their written consent. The study was conducted from 1 January 2010 to 30 May 2010.

The age range of participants ($n = 122$) was between 20 and 68 (mean age 37.7 ± 10.8). There were 87 women (mean age 37.7 ± 10.9 years) and 35 men (mean age 37.6 ± 10.7 years).

All the examined patients were interviewed using the questionnaire prepared by the authors which contained questions about age, education, professional activity, duration and course of the disease, treatment of MS, sleep disorders and the use of sleeping pills (see attachment). Subsequently, all of them completed the following questionnaires: Fatigue Severity Scale (FSS) [28], Epworth Sleepiness Scale (ESS) [29], Athens Insomnia Scale (AIS) [30], Hospital Anxiety and Depression Scale (HADS) [31] and Montgomery-Asberg Depression Rating Scale (MADRS) [32]. What is more, neurological examination was performed and the level of dis-

ability was established by use of Expanded Disability Status Stage (EDSS) by Kurtzke [33]. At the end, the course of SM was established (after analysis of the results from the questionnaire and neurological status).

The Fatigue Severity Scale (FSS) is a method of evaluating fatigue in different chronic diseases. The subject is asked to read nine statements (e.g. "Exercise brings on my fatigue", "Fatigue interferes with carrying out certain duties and responsibilities", "Fatigue interferes with my work, family, or social life") and circle a number from 1 to 7 for each of them, as appropriate depending on how he or she felt during the preceding week. A low value indicates that the statement is not very appropriate whereas a high value indicates agreement. The result is scored by adding up all the answers. A total of more than 36 points is considered to be abnormal and suggests fatigue [28].

The Epworth Sleepiness Scale (ESS) is a scale intended to measure daytime sleepiness. The subject is asked to rate the probability of falling asleep in eight different situations (e.g. watching television, reading, driving a car) on a scale of increasing probability from 0 to 3. The scores for the eight questions are added together to obtain a single number. A result between 0 and 9 points is considered to be normal while a result between 10 and 24 points indicates excessive daytime sleepiness [29].

The Athens Insomnia Scale (AIS) is a self-assessment psychometric instrument designed for quantifying sleep difficulty. It consists of eight items: the first five pertain to sleep induction, awakenings during the night, final awakening, total sleep duration, and sleep quality; the last three refer to the day-time symptoms well-being, functioning capacity, and sleepiness during the day. The responses are selected from four options: not a problem (0 points), slight problem (1 point), considerable problem (2 points), and could not sleep (3 points). The total score is obtained by adding up all the points. A score of 6 or more points indicates insomnia [30].

The Hospital Anxiety and Depression Scale (HADS) is a self-assessment screening questionnaire for anxiety and depression. The patients are asked to choose one response from the four given per each question. The questions relating to anxiety, marked with 'A' (7 questions), and to depression, marked with 'D' (7 questions), are given alternately. The scores (from 0 to 3) for each question for 'A' and separately for 'D' are added together to obtain two results: for anxiety and depression. A total score of 0 to 7 indicates no abnormality, 8-10 is borderline, and 11 and above suggests anxiety or depression [31].

The Montgomery-Asberg Depression Rating Scale (MADRS) is a ten-item diagnostic questionnaire used

to measure the severity of depression in patients. The items measure several dimensions of depressive symptoms such as apparent and reported sadness, inner tension, reduced sleep, reduced appetite, loss of concentration, lassitude, inability to feel, pessimistic thoughts and suicidal ideas. The MADRS divides the severity of symptoms into grades from 0 to 6. The result is obtained by adding up all the answers: 0-11 points indicates no abnormality, 12-19 – mild depressive symptoms, 20-28 – moderate depressive symptoms, 29-43 – severe depressive symptoms, 44-60 – very severe depressive symptoms.

For the purposes of this work, the linguistic adaptation of the scales was performed. First, each scale was translated from English into Polish by two independent translators, speaking fluent English, but for whom the Polish language was the mother tongue. Upon agreement on the common version, a reverse translation was done by two independent translators for whom English was the mother tongue. The reverse translation was performed to validate the Polish version of each scale.

Statistical analysis was performed using the program STATISTICA v.6. Data were expressed as mean \pm standard deviation (SD) or percentages. Because some scores did not fit a normal distribution, non-parametric tests were used. The analysis of correlation between results of the tests was done using Spearman correlation analysis and linear regression analysis. A *p* value of < 0.05 was taken as significant.

Results

The mean disease duration in the examined group was 6.7 ± 7.6 years. The course of MS was relapsing-remitting (RR) in 92 patients, and secondary progressive (SP) in 30 patients. The mean EDSS score was 2.2 ± 1.4 points. The patients were currently treated with interferon beta 1a (Avonex) – 3 persons, interferon beta 1b – 50 persons (Extavia – 19; Betaferon – 31), glatiramer acetate (Copaxone) – 14 persons, and mitoxantrone – 6 persons.

Self-reported education level was as follows: elementary – 6 patients, vocational – 24 patients, secondary – 54 patients, and high (university) – 38 patients. Among all the participants, there were 65 professionally active people, and 57 professionally inactive ones.

Fatigue was present in 75 MS patients (61.5%). Mean score in the FSS was 40.6 ± 14.8 points.

In the general questionnaire, sleep disorders were reported by 45 MS patients (37%). Nine of them used at least 1 sleeping pill per week.

Table 1. Correlation between results of used questionnaires (Spearman coefficient R, *p* – significance of correlation)

	FSS	ESS	AIS	HADS-D	HADS-A	MADRS
ESS	0.18	–	0.08	0.17	0.1	0.25
	<i>p</i> = 0.03		NS	<i>p</i> = 0.03	NS	<i>p</i> = 0.0003
AIS	0.2	0.08	–	0.35	0.4	0.41
	<i>p</i> = 0.014	NS		<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
FSS	–	0.18	0.2	0.33	0.33	0.32
		<i>p</i> = 0.03	<i>p</i> = 0.014	<i>p</i> = 0.0001	<i>p</i> = 0.0001	<i>p</i> = 0.00016
HADS-D	0.33	0.17	0.35	–	0.56	0.52
	<i>p</i> = 0.0001	<i>p</i> = 0.03	<i>p</i> < 0.0001		<i>p</i> < 0.0001	<i>p</i> < 0.0001
HADS-A	0.33	0.1	0.4	0.56	–	0.54
	<i>p</i> = 0.0001	NS	<i>p</i> < 0.0001	<i>p</i> < 0.0001		<i>p</i> < 0.0001
MADRS	0.32	0.25	0.41	0.52	0.54	–
	<i>p</i> = 0.00016	<i>p</i> = 0.003	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	

FSS – Fatigue Severity Scale, ESS – Epworth Sleepiness Scale, AIS – Athens Insomnia Scale, HADS-D – Hospital Anxiety and Depression Scale for assessment of depressive symptoms, HADS-A – Hospital Anxiety and Depression Scale for assessment of anxiety, MADRS – Montgomery-Asberg Depression Rating Scale, NS – non-significant

Excessive daytime sleepiness was present in 25 MS patients (20.5%). Mean score in the ESS was 6.3 ± 3.9 points.

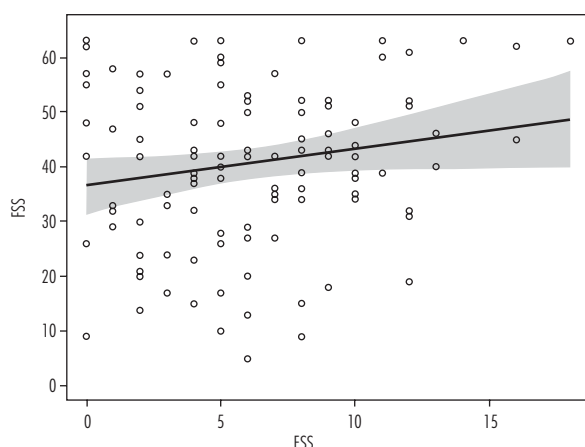
Insomnia was recognized in 73 MS patients (59.8%), including mild symptoms in 30 (24.6%), and clinically significant symptoms in 43 individuals (35.2%). Mean AIS score was 8.4 ± 5.7 points.

According to MADRS, depression was diagnosed in 33 MS patients (27%): mild symptoms were present in 20 individuals (14.4%), moderate in 10 (8.2%), and severe in 3 (2.5%). Mean MADRS score was 9.4 ± 7.9 points.

According to HADS, depressive symptoms were present in 15 MS patients (12.3%), and 17 persons achieved a borderline result (13.9%). Mean HADS-D score was 5.5 ± 3.6 points.

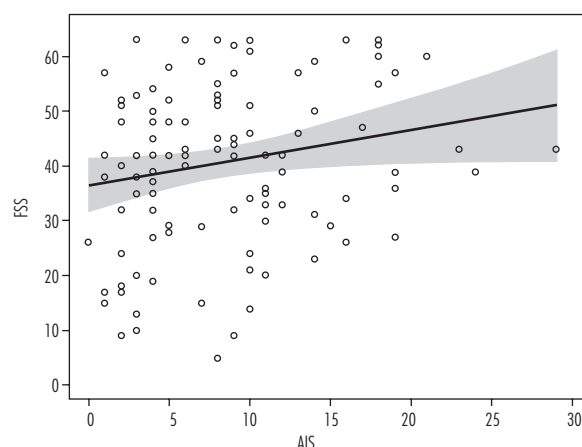
Anxiety was present in 32 MS patients (26.2%), and 37 persons achieved a borderline HADS-A score (30.3%). Mean HADS-A result was 8.4 ± 3.7 points.

A weak correlation was observed between fatigue (FSS) and sleep disorders (ESS, AIS) (Table 1, Figs. 1 and 2). A stronger correlation was present between fatigue (FSS) and either depression (MADRS, HADS-D) or



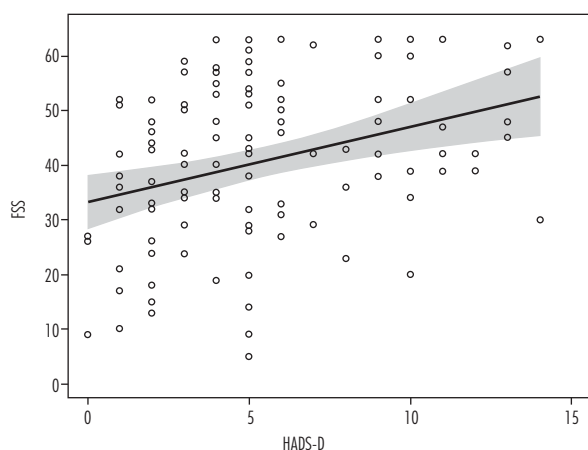
FSS – Fatigue Severity Scale, ESS – Epworth Sleepiness Scale

Fig. 1. The relationship between fatigue (FSS) and excessive daytime sleepiness (ESS) (linear regression analysis: $R^2 = 0.02$; $p = 0.06$)



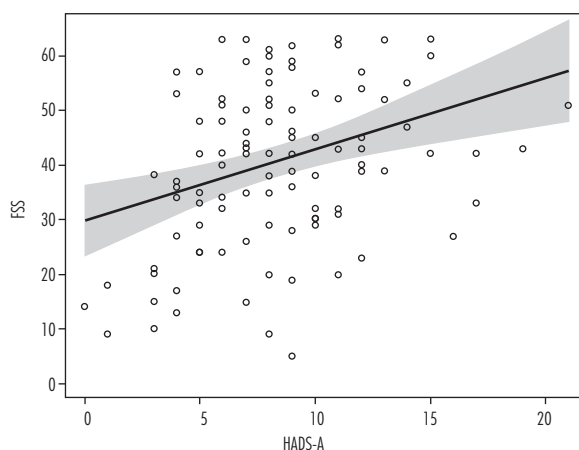
FSS – Fatigue Severity Scale, AIS – Athens Insomnia Scale

Fig. 2. The relationship between fatigue (FSS) and insomnia (AIS) (linear regression analysis: $R^2 = 0.03$; $p = 0.04$)



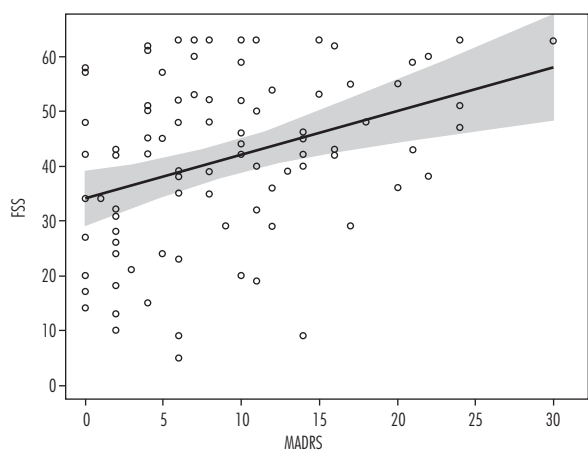
FSS – Fatigue Severity Scale, HADS-D – Hospital Anxiety and Depression Scale for assessment of depressive symptoms

Fig. 3. The relationship between fatigue (FSS) and depressive symptoms (HADS-D) (linear regression analysis: $R^2 = 0.1$; $p < 0.01$)



FSS – Fatigue Severity Scale, HADS-A – Hospital Anxiety and Depression Scale for assessment of anxiety

Fig. 4. The relationship between fatigue (FSS) and anxiety symptoms (HADS-A) (linear regression analysis: $R^2 = 0.1$; $p < 0.01$)



FSS – Fatigue Severity Scale, MADRS – Montgomery-Asberg Depression Rating Scale

Fig. 5. The relationship between fatigue (FSS) and depressive symptoms (MADRS) (linear regression analysis: $R^2 = 0.12$; $p < 0.01$)

anxiety (HADS-A) (Table 1, Figs. 3-5). A significant correlation was also found between sleep disorders (ESS, AIS) and depression (MADRS, HADS-D). Anxiety was only associated with presence of insomnia (AIS), not excessive daytime sleepiness (ESS). A significant correlation was observed between results of questionnaires assessing depressive symptoms (MADRS and HADS-D), and also between those assessing anxiety (HADS-A) and depression (MADRS, HADS-D) (Table 1).

The FSS score was not associated with age, sex, disease course and duration, EDSS, treatment or level of education in MS patients. However, in professionally inactive people we observed significantly higher FSS scores

(44.8 ± 13.8) in comparison with active individuals (37.2 ± 14.9 ; $p = 0.0053$).

A higher AIS score, but not ESS score, was associated with longer duration of the disease ($p = 0.0001$), female sex (9.2 ± 5.7 vs. 6.5 ± 3.9 in men; $p = 0.006$) and professional inactivity (9.9 ± 5.5 vs. 6.9 ± 5.2 in active professionally; $p = 0.0015$). Age, level of education, EDSS and disease course influenced neither AIS nor ESS scores.

Results of questionnaires assessing depressive symptoms correlated significantly with age ($p = 0.006$ for MADRS; $p < 0.0001$ for HADS-D). Level of education influenced only HADS-D scores ($p = 0.002$). Professionally inactive people had significantly higher MADRS (11.6 ± 7.6 vs. 7.6 ± 6.3 ; $p = 0.0013$) and HADS-D scores (6.5 ± 3.9 vs. 4.7 ± 3.1 ; $p = 0.004$) than active individuals. Disease duration and course, EDSS and sex did not influence the MADRS and HADS-D scores.

The HADS-A score correlated with age ($p = 0.005$), but not with education, disease duration or EDSS. The HADS-A results were significantly higher in professionally inactive MS patients (9.2 ± 3.6) in comparison with active ones (7.7 ± 3.7 ; $p = 0.02$).

Patients treated with interferon beta had significantly lower MADRS scores (7.6 ± 6.6) than untreated individuals (12.2 ± 9.8 ; $p = 0.023$). Also, subjects treated with glatiramer acetate had significantly lower MADRS scores (8.8 ± 6.2) in comparison with untreated ones (12.2 ± 9.8 ; $p = 0.04$). The results of other tests did not differ significantly between these two groups (Table 2).

Table 2. Association between results of questionnaires and other factors: age, sex, education, disease duration and course, EDSS, treatment, and professional activity (*p*-value)

	FSS	ESS	AIS	HADS-D	HADS-A	MADRS
Age	NS	NS	NS	$p < 0.0001$	$p = 0.005$	$p = 0.0006$
Sex (F vs. M)	NS	NS	$p = 0.006$	NS	0.03	NS
Education	NS	NS	NS	$p = 0.002$	NS	NS
Disease duration	NS	NS	$p = 0.0001$	NS	NS	NS
Multiple sclerosis course (RR vs. SP)	NS	NS	NS	NS	NS	NS
EDSS	NS	NS	NS	NS	NS	NS
Treated with interferon beta vs. untreated	NS	NS	NS	NS	NS	$p = 0.023$
Treated with glatiramer acetate vs. untreated	NS	NS	NS	NS	NS	$p = 0.04$
Professional activity (active vs. non-active)	$p = 0.0053$	NS	$p = 0.0015$	$p = 0.004$	$p = 0.02$	$p = 0.0013$

FSS – Fatigue Severity Scale, ESS – Epworth Sleepiness Scale, AIS – Athens Insomnia Scale, HADS-D – Hospital Anxiety and Depression Scale for assessment of depressive symptoms, HADS-A – Hospital Anxiety and Depression Scale for assessment of anxiety, MADRS – Montgomery-Asberg Depression Rating Scale, F – female, M – male, RR – relapsing remitting, SP – secondary progressive course, EDSS – Expanded Disability Status Scale

Discussion

According to literary resources, up to 90% of MS patients could suffer from fatigue [5,28]. The results of our study have confirmed it. We observed fatigue among 61.5% of the examined MS patients. What was reported by other authors, and also appeared in our study, was the fact that the frequency of fatigue was independent of sex and age [6]. Although some investigators observed a correlation between fatigue and EDSS or disease duration [34,35], we could not confirm it, similarly to other researchers [7]. We also did not observe an association between fatigue and disease course, although some authors noted that fatigue appeared to be more severe among patients with progressive MS [36,37].

The pathophysiology of fatigue in MS is not well known. Identifying factors that play an important role in fatigue in MS would improve its care and treatment. Some authors have observed a close relation between fatigue and sleep disorders [4,7,15,38,39]. Recently, Veauthier *et al.* examined 66 MS patients using the Modified Fatigue Impact Scale and polysomnography, and found a clear and significant association between fatigue and sleep disorders: 96% of fatigued MS individuals suffered from sleep disturbances (in comparison to 60% of non-fatigued ones) [21]. Conversely, suffering from sleep disorders was associated with an increased risk of fatigue. The results of our study also confirmed it. Excessive daytime sleepiness which is a symptom of sleep disturbances could not be distinguished from fatigue.

On the other hand, either sleep disorders or fatigue may exacerbate other MS symptoms, and have a great impact on mental and physical activity, quality of life, work productivity and utilization of health care services [2,40,41]. The quality of sleep is especially important to people with MS because recent studies suggest that good sleep is necessary for proper brain function and plasticity. According to some authors, slow wave sleep is important for downscaling the synaptic strength of new brain circuits being a consequence of the plastic process to energetically sustainable baseline level, good for learning and memory [2,42]. This plasticity is very important for MS patients to maintain physical and mental function [43]. This is why it is so important to recognize and treat sleep disorders in MS patients. It may be true that improving sleep quality will also influence cognitive and psychosocial functioning, as well as fatigue in MS.

It is also interesting that although 36% of examined MS patients reported sleep disturbances, only 7.4% used sleeping pills at least once a week. It is similar to the level reported in the general population in the USA [44,45], but less than in the group of MS patients [2]. Bamer *et al.* reported that 36% of MS individuals used prescription or over-the-counter sleep medication at least 1-2 times a week [2].

The other factor that may play an important role in aetiology of fatigue is depression. Some authors have observed a relation between fatigue and depression [2,17]. Our present and previous study [46] also confirms it. However, there are also reports that depression and fatigue

constitute two different disorders [47,48], since it was noticed that fatigue – but not depression – could decrease in low temperatures, after a night sleep or rest. Furthermore, fatigue may appear episodically, while depression is more persistent. These conflicting results may be due to the use of different methods and questionnaires to diagnose both fatigue and depression.

Similarly to other authors [37,49], we found that immunomodulating therapy was not associated with fatigue. Some researchers have reported that such therapy could induce or intensify sleep disorders [22] but our study did not confirm it. We found no association between therapy and the results of most questionnaires. We only observed a relationship between immunomodulating therapy and MADRS results: people treated with either beta-interferon or glatiramer acetate had a significantly lower score than untreated individuals. Other recent studies also suggest that interferon beta therapy neither causes nor exacerbates depression among MS patients [50, 51], but there are also reports about an association between such therapy and mood disorders [52,53].

One of the factors influencing the results of our study was professional activity. MS patients who were professionally inactive had significantly higher scores in most applied questionnaires. This result suggested that a professionally active lifestyle could be protective against fatigue, insomnia, anxiety and depression. Consequently, MS patients who do not work are at greater risk of developing either sleep and mood disorders or fatigue. The doctors and nurses taking care of MS patients should encourage them to work as long as possible.

All the MS patients examined in this study currently live and stay in Silesia, an industrial region which is still considered to be one of the most polluted in Poland. It is reported that air pollution could lead to various health problems, including fatigue. Further comparative studies in Poland are needed to establish whether habitation has a real impact on fatigue in MS.

Further larger prospective studies are also needed to establish the role of sleep and mood disorders in the development of fatigue in MS. It should be documented if the treatment of concomitant sleep disorders and depression has had a significant impact on fatigue in MS.

Conclusions

1. Fatigue is a very common symptom in MS, sometimes associated with sleep disorders, depression or anxiety.

2. Fatigue should be considered in every patient with MS, independently of age, sex, level of education, disability, treatment, disease duration and course.
3. Professionally inactive MS patients suffer more often from fatigue, insomnia and mood disorders than active ones.
4. The treatable causes of fatigue in MS such as sleep and mood disturbances should be identified and treated.

Disclosure

Authors report no conflict of interest.

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Appendix

Questionnaire for the patient:	
1. Name	
2. Age	
3. Sex (underline)	
Female	
Male	
4. Education (underline):	
Elementary	
Vocational	
Secondary	
High (university)	
5. Professional activity (underline):	
Active	
Non-active	
6. Date of diagnosis of SM	
7. Date of first symptoms of SM	
8. Date of last relapse	
9. Number of relapses in the last year	
10. Course of the disease	
11. Symptoms (interview).....	
12. Current treatment of MS	
13. Previous treatment of MS	
14. Other drugs used	
15. Problems with sleep (underline):	
No problems	
Insomnia	
Excessive daytime sleepiness	
Other	
16. Have you ever used sleeping pills? (underline)	
Never	
Occasionally, but less than once a week	
At least once a week	