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Association Between Sleep Quality and Clinical-Cognitive Parameters in Multiple Sclerosis: A Multidisciplinary Cross-Sectional Study

Multipl Sklerozda Uyku Kalitesi ile Klinik-Bilişsel Parametreler Arasındaki İlişki: Multidisipliner Kesitsel Bir Çalışma

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Abstract

Objective: Sleep disturbances are a common symptom among patients with multiple sclerosis (MS). The Pittsburgh Sleep Quality Index (PSQI) is a reliable and practical tool for assessing sleep quality. The present study examined the association between sleep quality and clinical and radiologic characteristics in individuals with MS.

Materials and Methods: In this retrospective study, 137 patients with MS (PwMS) were included following stringent clinical, radiologic, and psychiatric exclusion criteria. Demographic, clinical, cognitive, and neuroimaging data were extracted from medical records. Sleep quality was assessed using the PSQI, with a global score ≥5 indicating poor sleep quality.

Results: Among the 137 PwMS, no significant differences were observed in demographic, clinical, cognitive, or radiologic parameters between those with good and poor sleep quality. However, walking speed was significantly slower in poor sleepers (p=0.005). Sleep onset latency and subjective sleep quality were strongly correlated with overall PSQI scores. In contrast, lesion location, corpus callosum index, and measures of brainstem or spinal cord atrophy showed no association with sleep quality.

Conclusion: Sleep quality is adversely affected in PwMS and correlates with lower-limb physical performance. Patients' self-assessments of sleep quality appear consistent. Prolonged sleep onset latency is an important factor, while the effects of sleep duration and disturbance are less significant.

Keywords: Multiple sclerosis, sleep quality, Pittsburgh Sleep Quality Index, magnetic resonance imaging, physical performance, cognitive function, sleep latency

Öz

Amaç: Uyku bozuklukları, multipl skleroz (MS) hastalarında sık görülen bir semptomdur. Pittsburgh Uyku Kalitesi Endeksi (PSQI), uyku kalitesini değerlendirmek için güvenilir ve pratik bir araçtır. Bu çalışma, MS hastalarında uyku kalitesi ile klinik ve radyolojik özellikler arasındaki ilişkileri incelemiştir.

Gereç ve Yöntem: Bu retrospektif çalışmada, sıkı klinik, radyolojik ve psikiyatrik dışlama kriterleri doğrultusunda 137 MS hastası (PwMS) dahil edildi. Demografik, klinik, bilişsel ve nörogörüntüleme verileri tıbbi kayıtlardan çıkarıldı. Uyku kalitesi PSQI kullanılarak değerlendirildi ve genel puan ≥5 olanlar kötü uyku kalitesine sahip olarak kabul edildi.

Bulgular: Yüz otuz yedi MS hastası arasında, iyi ve kötü uyku kalitesine sahip olanlar arasında demografik, klinik, bilişsel veya radyolojik parametrelerde anlamlı bir fark gözlenmedi. Ancak, kötü uyuyanlarda yürüme hızı anlamlı olarak daha yavaştı (p=0,005). Uykuya dalma süresi ve öznel uyku kalitesi, genel PSQI puanları ile güçlü bir korelasyon gösterdi. Buna karşın, lezyonun yeri, korpus kallosum indeksi ve beyin sapı veya omurilik atrofisi ölçümleri uyku kalitesi ile herhangi bir ilişki göstermedi.

Sonuç: MS hastalarında uyku kalitesi olumsuz etkilenir ve alt ekstremite fiziksel performansı ile ilişkilidir. Hastaların uyku kalitesine ilişkin öz değerlendirmeleri tutarlı görünmektedir. Uykuya dalma süresinin uzaması önemli bir faktördür, ancak uyku süresi ve uyku bozukluğunun etkileri daha az önemlidir.

Anahtar Kelimeler: Multipl skleroz, uyku kalitesi, Pittsburgh Uyku Kalitesi Endeksi, manyetik rezonans görüntüleme, fiziksel performans, bilişsel işlev, uyku latansı

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Introduction

Multiple sclerosis (MS), a chronic inflammatory and neurodegenerative disease of the central nervous system (CNS), is a multifaceted condition that has a profound impact on individuals, caregivers, and the healthcare system.[1] MS is characterized by various clinical symptoms in the CNS, including gait changes, spinal cord symptoms, motor and sensory deficits, cranial nerve dysfunction, speech disorders, cognitive deficits, fatigue, and sleep disturbances.[2] Sleep disturbance is one of the factors that can affect the quality of life of patients with MS (PwMS).[3-8] Many factors probably contribute to sleep disorders. They may be due to other comorbidities or medications, as well as the involvement of brain nuclei that regulate sleep.

The Pittsburgh Sleep Quality Index (PSQI) questionnaire, which reflects an overall assessment of sleep quality over the past month, is convenient and valuable for PwMS. This study aimed to investigate the relationship between sleep quality and its components and demographic, clinical, and radiologic characteristics in PwMS.

Materials and Methods

Patient Selection

In this study, we retrospectively reviewed 628 medical records of patients with a definitive diagnosis of MS, according to the revised McDonald 2017 diagnostic criteria, who were evaluated for sleep quality using the PSQI at our center between December 2022 and May 2024. This study was conducted with the approval of the Bursa Uludağ University Clinical Research Ethics Committee (approval number: 2025/700-11/10, date: 11.06.2025). The date on which sleep quality was assessed was used as the baseline. The presence of incidental lesions unrelated to MS on magnetic resonance imaging (MRI), contrast-enhancing demyelinating lesions, a demyelinating relapse or steroid use within the previous month, use of medications that could affect sleep quality, comorbid conditions, the presence of clinically significant depressive symptoms determined by the Geriatric Depression Scale (GDS) or Beck Depression Inventory (BDI) administered concurrently. Patients with progressive MS were excluded from the study. Data from 137 eligible patients were included; see the patient selection flowchart for details (Figure 1).

Clinical and Radiologic Assessments

Demographic data, disease duration, number of attacks, average annual relapse [relapse count/year(s)], Expanded Disability Status Scale (EDSS) score, and most recent disease modifying treatments (DMTs) and their duration were obtained from clinical records based on assessments by three independent neurologists with experience in MS. Results of the montreal cognitive assessment (MoCA) and its components, the symbol-digit modalities test (SDMT), BDI, GDS, the nine-hole-peg test (9HPT), and the timed 25-foot walk test (T25-FW), administered by the same psychologist with experience in neurology, were obtained from patient records. Global PSQI scores and subscale scores (administered intermittently during routine patient follow-up) were retrospectively evaluated by a neurologist who was experienced in sleep disorders.

All examinations were performed on a 1.5T MRI scanner (Aera®, Siemens, Erlangen, Germany). MRI included fluid attenuated inversion recovery, T1-, T2-, diffusion-weighted images in the axial and sagittal planes, with and without contrast, were obtained using standard parameters (repetition time: 576 ms, echo time: 8 ms, slice thickness: 5 mm, slice spacing: 6 mm, flip angle: 90°). The localization of demyelinating lesions (cortical/subcortical, periventricular, infratentorial, temporal, corpus callosum, spinal cord), the presence of coalescing lesions, and

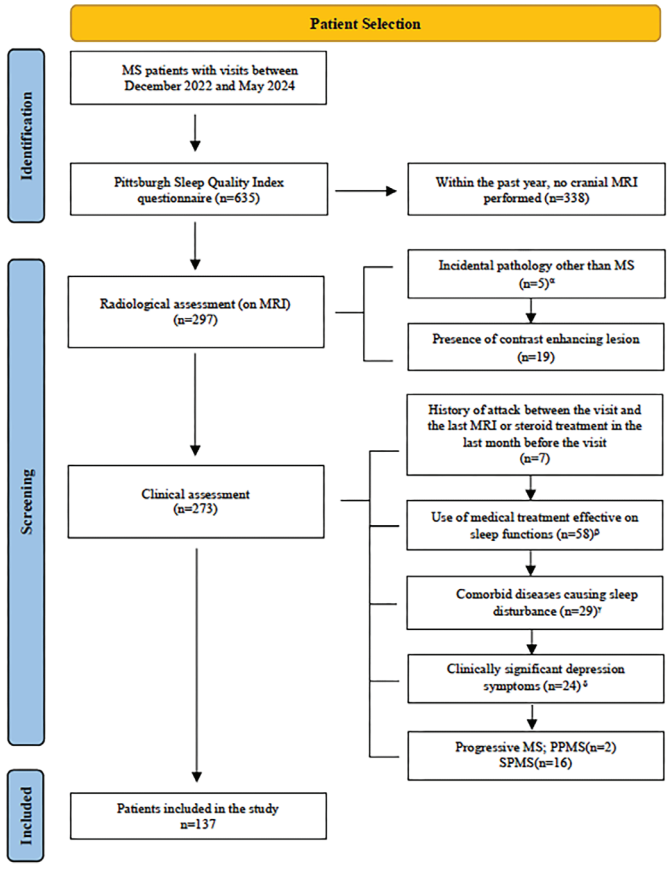

Figure 1. Patient selection flowchart

†Venous anomaly (n=1), hemangioma (n=1), hydrocephalus (n=1), syrinx (n=2)

‡Use of any dose of sleeping pills, antidepressants, psychotropic or gabapentanoids

§Thyroid disease (n=8), psychiatric disorders (n=7), cardiovascular diseases (n=5), diabetes (n=3), hematologic diseases (n=2), epilepsy (n=1), asthma (n=1), rheumatologic disease (n=1), lumbar disc herniation (n=1)

¶Determined by administering the Geriatric Depression Scale (GDS) or the Beck Depression Inventory (BDI) simultaneously with assessing sleep. Clinically significant depression (≥17 for BDI, ≥5 for GDS) on the BDI (for patients aged <65 years) and the GDS (for patients aged ≥65 years).

MS: Multiple sclerosis MRI: Magnetic resonance imaging, PPMS: SPMS:

measurements of atrophy of the corpus callosum, brainstem, and spinal cord were performed and recorded by two research assistants at sites determined by the joint decision of two radiologists experienced in neurology (see Appendices 1 and 2 for measurement methods and examples).

Patients with global PSQI scores of ≥5 were grouped as those with poor sleep quality. The results were analyzed using demographic, clinical, and radiologic parameters.

Statistical Analysis

Whether the data showed normal distribution was analyzed using the Shapiro-Wilk test. Descriptive statistics are expressed as means and standard deviations or medians (minimum-maximum) for quantitative data, and frequencies and percentages for qualitative data. For normally distributed data, one-way analysis of variance was used in the comparison of more than two groups, and the Kruskal-Wallis test was used for non-normally distributed data. The Mann-Whitney U test was used for non-normally distributed data in two independent group comparisons. Categorical data were analyzed using Pearson's chi-square test, the Fisher-Freeman-Halton test, and Fisher's exact chi-square test. In case of significance, the Bonferroni test, one of the multiple comparison tests, was used. The relationships between variables were analyzed using the Pearson or Spearman correlation coefficient. The significance level was set as α=0.05. Statistical data analysis was performed using the IBM SPSS 28.0 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.) statistical package program and graphs were generated using Minitab® Statistical Software v.19.

Results

The mean age of the 137 patients, 106 females and 31 males, was 38.51 (range, 18-67) years, and the mean duration of the disease was 6.68 (range, 0-25) years. Of the patients enrolled in the study, 106 were measured for body mass index (BMI), 135 were measured for cervical MRI, and 55 were measured for thoracic MRI. The SDMT was performed concurrently in 110 patients. MoCA, T25-FW, and 9HPT results were available for 111 patients. The mean BMI was 24.79 (range, 16.6-42.8) kg/m^2, the mean duration of DMT use 3.54 (range, 0-18) years, the mean EDSS score was 1.28 (range, 0-6), and the average annual relapse rate was 0.45 (range, 0.07-2). Platform and second-line DMTs were used in most patients.

According to the global PSQI, there were no significant differences between patients with good and poor sleep quality regarding age, sex, BMI, disease or DMT use duration, DMTs used, average annual relapse rates, and EDSS MoCA, and SDMT scores. There was no significant difference in upper extremity function. However, walking speed was slower in those with poor sleep quality (p=0.005) (Table 1, Figure 2).

Fifty-three patients did not have a roommate according to the PSQI. Twelve patients reported long intervals between breaths during sleep, 15 reported at least one twitching or jerking of the legs while sleeping, and one reported disorientation or confusion. There was no difference in global PSQI scores and sleep quality between those who reported snoring, restless legs symptoms, and sleep apnea in the PSQI questionnaire (p=0.441, p=0.524, and p=0.406, respectively). All seven subscales of the PSQI, especially sleep onset latency and subjective sleep quality r=0.786 and r=0.767, respectively, showed a positive correlation with an increase in total PSQI scores in all patients. However, sleep duration and sleep disturbances were not correlated with the global score in patients with poor sleep quality (p=0.249 and p=0.051, respectively) (Figure 3).

No association was found between lesion location, corpus callosum index (CCI), brainstem or spinal cord atrophy measures, and poor sleep quality (Tables 2 and 3).

Discussion

Sleep disturbance is one of the factors that can affect the quality of life in PwMS. They are more common in PwMS than in the general population, with no significant difference between the sexes (about 40% vs. 60-75%).[3-8] Sleep disturbances are commonly reported in secondary progressive MS. The frequency and severity of sleep disturbances may increase with age, disease duration, number of relapses, and disability levels.[5,9-11] Sleep disturbances in MS are likely multifactorial. They may be due to the involvement of brain nuclei, which regulates sleep, as well as pain, fatigue, depression/anxiety, intrinsic sleep disturbances, and pharmacologic treatments.[8] The presence of other comorbidities (especially depression) or an increased number of comorbidities is associated with poorer sleep quality and a higher global PSQI scores.[12]

This study found no statistically significant relationship between demographic characteristics, basic clinical characteristics of the disease, and sleep quality in PwMS. This situation confirms that the main confounding factors were excluded, in line with the aim of our study to identify the main components that might affect sleep quality in PwMS and the effect of lesion localization and characterization.

Sleep disturbances in PwMS may result from a common biologic link that affects sleep homeostasis, such as circadian rhythm disruption, decreased melatonin secretion, and increased levels of proinflammatory cytokines. Reduced sleep quality and sleep-related disorders may reflect underlying biologic and molecular changes associated with neuroinflammation, neurodegeneration, and white matter lesion burden.[5,13-15] sleep disorders have been associated with increased lesion burden.[16] Patients with neuromyelitis optica spectrum disorder with more severe demyelination have poorer sleep quality and use more sleeping pills than PwMS.[10] In our study, we found no significant differences in the sleep quality in PwMS. Average annual relapses, another clinical indicator of inflammation, also showed no differences. These results may have been influenced by excluding patients with inflammatory activity (new relapses or contrast-enhancing demyelinating lesions) during patient selection. More light will be shed on this issue in studies with larger numbers of patients that also assess relapses.

Sleep is closely associated with fatigue, mood, cognitive function, and physical performance.[17] Poor sleep reduces the ability to perform daily activities and impairs social communication skills,

Table 1. The relationship between clinical characteristics, cognitive and physical function tests

Demographic and clinical characteristics		Total	Good	Poor	p
Sex, n (%),	female male	106 (77.4) 31 (22.6)	73 (78.5) 20 (21.5)	33 (75) 11 (25)	0.649
Age		38.51 (10.98), 38 (18-67)	37.7 (10.42), 36 (19-61)	40.22 (12.02), 42 (18-67)	0.212
BMI		24.79 (4.76), 23.9 (16.6-42.8)	24.72 (4.6), 23.98 (16.6-37.5)	24.94 (5.14), 23.69 (17.7-42.8)	0.879
Disease duration, years		6.68 (5.49), 5 (0-25)	6.36 (5.58), 5 (0-25)	7.36 (5.28), 6.5 (0-22)	0.320
Duration of DMT use, years		3.54 (3.56), 2 (0-18)	3.38 (3.47), 2 (0-17)	3.89 (3.8), 3 (0-18)	0.322
EDSS		1.28 (1.01), 1 (0-6)	1.17 (0.91), 1 (0-5)	1.5 (1.19), 1 (0-6)	0.075
Average annual relapse		0.45 (0.35), 0.33 (0.07-2)	0.47 (0.39), 0.33 (0.07-2)	0.4 (0.23), 0.33 (0.1-1)	0.703
DMTs	Naive	8 (5.8)	7 (7.5)	1 (2.3)	0.901
	Interferon beta 1	14 (10.2)	10 (10.8)	4 (9.1)	
	Glatiramer acetate	18 (13.1)	11 (11.8)	7 (15.9)	
	Teriflunomide	37 (27)	23 (24.7)	14 (31.8)	
	Dimethyl fumarate	23 (16.8)	16 (17.2)	7 (15.9)	
	Fingolimod	26 (19)	20 (21.5)	6 (13.6)	
	Cladribine	7 (5.1)	3 (3.2)	4 (9.1)	
	Azathioprine	1 (0.7)	1 (1.1)	-	
	Natalizumab	1 (0.7)	-	1 (2.3)	
	Alemtuzumab	1 (0.7)	1 (1.1)	-	
	Rituximab	1 (0.7)	1 (1.1)	-	
MoCA	Visuospatial & executive (/5)	4.42 (2.79), 4 (1-30)	4.57 (3.28), 5 (1-30)	4.1 (0.96), 4 (1-5)	0.356
	Naming (/3)	2.64 (0.48), 3 (2-3)	2.62 (0.49), 3 (2-3)	2.67 (0.48), 3 (2-3)	0.681
	Attention (/6)	4.71 (1.38), 5 (1-6)	4.68 (1.42), 5 (1-6)	4.77 (1.3), 5 (2-6)	0.840
	Language (/3)	1.6 (1.12), 2 (0-3)	1.62 (1.13), 2 (0-3)	1.53 (1.14), 2 (0-3)	0.711
	Abstraction (/2)	1.73 (0.59), 2 (0-2)	1.75 (0.55), 2 (0-2)	1.67 (0.66), 2 (0-2)	0.571
	Delayed recall (/5)	2.98 (1.31), 3 (0-5)	3 (1.28), 3 (0-5)	2.93 (1.39), 3 (0-5)	0.987
	Orientation (/6)	5.97 (0.17), 6 (5-6)	5.97 (0.17), 6 (5-6)	5.97 (0.18), 6 (5-6)	0.908
	Total	23.53 (4.05), 24 (11-30)	23.53 (4.11), 24 (11-30)	23.55 (3.96), 24 (13-29)	0.918
SDMT		33 (13.48), 35 (1-57)	32.81 (13.15), 35 (1-57)	31.06 (14.24), 34 (4-54)	0.330
9HPT	Right	19.98 (3.81), 19 (13-34)	20.03 (4.02), 20 (13-34)	19.89 (3.32), 19 (15-29)	0.854
	Left	21.59 (4.28), 21 (16-36)	21.73 (4.39), 21 (16-36)	21.27 (4.05), 20 (16-31)	0.641
T25-FW		7.79 (1.59), 6.5 (3.5-12)	6.52 (1.54), 6.5 (3.5-12)	7.45 (1.56), 7.5 (4.5-11.5)	**0.005**

Mean (SD), Median (min-max), or n (%).

DMT: Disease-modifying treatment, EDSS: Expanded Disability Status Scale, MoCA: Montreal cognitive assessment, SDMT: Symbol-digit modalities test, 9HPT: Nine-hole-peg test, SD: Standard deviation

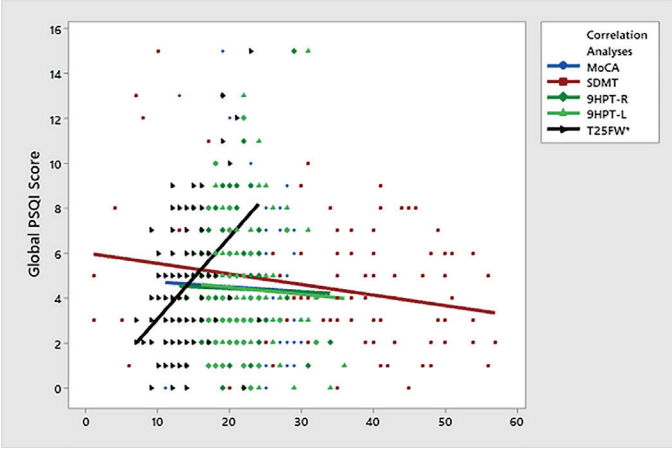

Figure 2. Correlation analysis between sleep quality index score and cognitive, and upper and lower extremity functions.
*p<0.05.
9HPT: Nine-Hole Peg Test (R:right, L:left), T25FW: Timed 25-foot walk test, MoCA: Montreal Cognitive Assessment, SDMT: the Symbol-digit modalities test and PSQI: Pittsburgh Sleep Quality Index PHPT-L: sor

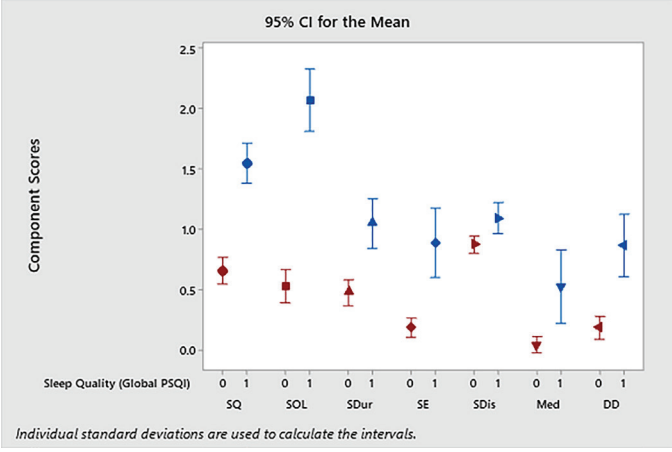

Figure 3. Changes in PSQI components according to sleep quality. When analyzing the correlation between the total score and the lower PSQI components in patients with poor sleep quality, all parameters showed a high correlation with the total score (p<0.001). In descending order, the parameters were SOL (r=0.786), SQ (r=0.767), SD (r=0.539), DD (r=0.528), SE (r=0.480), Med (r=0.440), and SDis (r=0.377). However, when analyzing patients with poor sleep quality, there was no significant correlation for SDur and SDis. For the other parameters, in descending order: Med (r=0.696, p<0.001), SQ (r=0.541, p<0.001), SOL (r=0.402, p=0.007), SE (r=0.320, p=0.034), and DD (r=0.302, p=0.046). Sleep Quality (Global PSQI); poor: 0 (red) and good: 1 (blue).
SQ: Sleep quality, SOL: Sleep onset latency, SDur: Sleep duration, SE: Sleep efficiency, SDis: Sleep disturbance, Med: Use of sleeping medications, DD: Daytime dysfunction,
PSQI: Pittsburgh Sleep Quality Index, SD: Standard deviation CI: Confidence interval

negatively impacting quality of life.[18] A correlation has been reported between sleep efficiency and number of awakenings after falling asleep, and stride length, stride speed, and stride duration.[19] The exact mechanism by which sleep affects walking is still not fully understood. However, one possible mechanism is degeneration in neuroanatomic regions that regulate sleep and walking, including the pontine tegmentum and pedunculopontine nuclei.[20,21] In addition, inadequate removal of metabolic waste from the brain due to sleep disturbances and creating a catabolic environment in skeletal muscles may reduce the effect of cognitive decline on gait mechanics and postural control, thereby worsening outcomes.[19,22,23] Most studies examining the relationship between sleep quality parameters and objective walking measurements have been conducted on healthy individuals, and the results vary.[24,25] Some studies found a positive correlation between sleep efficiency and walking speed, gait performance, and physical activity. However, other studies detected no such relationship, and the results vary.[24,26-28] The general consensus is that sleep quality is associated with walking speed, especially among older individuals. Further studies on the younger population are needed.[25]

Studies on PwMS have shown that sleep efficiency is related to step length. Additionally, walking speed and step duration are related to other sleep parameters independently of age.[19] Research on this topic in our country is quite limited. Some data exist on the connection between sleep quality and more indirect indicators, such as physical activity level and number of steps taken. One study of the general Turkish population found no significant relationship between sleep quality and daily step count or physical activity level.[29] A recent study of a small group of PwMS found an association between sleep quality and the six-minute walk test.[30] In our study, no difference was found in SDMT or MoCA scores in cognitive assessment based on sleep quality. In terms of physical performance, no difference was observed in finger dexterity scores (9HPT). In contrast, lower extremity performance (T25-FW) was worse in those with poor sleep quality, consistent with the literature cited above. Our demonstration of this result in a much larger cohort of PwMS, after thorough pre-screening and filtering out potentially confounding factors, is a valuable contribution to the literature. No significant association has been reported between the use or non-use of DMT, the type of use, the timing of use, or compliance problems and sleep quality in PwMS.[10,31,32] However, DMTs with different activity levels and mechanisms may have differences in sleep quality. Natalizumab and ocrelizumab may positively affect sleep quality, whereas interferon beta and glatiramer acetate may have a negative effect.[33-36] It is known that reducing systemic inflammation by suppressing NF-κB signaling, which dimethyl fumarate has a mild effect on, has an impact on sleep quality.[13,37] We found no difference in DMT distribution according to sleep quality. Further studies evaluating a larger cohort are needed in this regard.

Studies evaluating sleep architecture and components of sleep quality in PwMS have shown that patients with longer disease duration or greater disability tend to have lower sleep efficiency, shorter total sleep time, less nocturnal restfulness, longer sleep

Table 2. The relationship between lesion localization and sleep quality						
Lesion localization			**n**	**Sleep quality**		**p**
Good			**poor**			
Periventricular		Yes	130	87 (93.5)	43 (97.7)	0.301
No		7	6 (6.5)	1 (2.3)		
Temporal		Yes	53	36 (38.7)	17 (38.7)	0.993
No		84	57 (61.3)	27 (61.4)		
Cortical/juxtacortical		Yes	112	78 (83.9)	34 (77.3)	0.352
No		25	15 (16.1)	10 (22.7)		
Corpus callosum		Yes	45	26 (28)	19 (43.2)	0.078
No		92	67 (72)	25 (56.8)		
Infratentorial	Infratentorial	Yes	54	36 (38.7)	18 (40.9)	0.806
		No	83	57 (61.3)	26 (59.1)	
	Bulbus	Yes	14	10 (10.8)	4 (9.1)	0.765
		No	123	83 (89.2)	40 (90.9)	
	Pons	Yes	27	21 (22.8)	6 (13.6)	0.210
		No	109	71 (77.2)	38 (86.4)	
	Pontocerebellar peduncle	Yes	18	15 (16.1)	3(6.8)	0.133
		No	119	78 (83.9)	41 (93.2)	
	Mesencephalon	Yes	13	9 (9.7)	4 (9.1)	0.913
		No	124	84 (90.3)	40 (90.9)	
	Cerebellum	Yes	29	18 (19.4)	11 (25.6)	0.411
		No	107	75 (80.6)	32 (74.4)	
	Thalamus	Yes	5	5 (5.5)	-	0.123
		No	128	86 (94.5)	42 (100)	
Spinal cord	Cervical	Yes	89	62 (67.4)	27 (62.8)	0.601
		No	46	30 (32.6)	16 (37.2)	
	Thoracic	Yes	19	15 (38.5)	4 (25)	0.345
		No	36	24 (61.5)	12 (75)	
Other	Coalescing lesions	Yes	16	11 (11.8)	5 (11.4)	0.937
		No	121	82 (88.2)	39 (88.6)	
There were no statistically significant differences between patients with good and poor sleep quality based on the location of the demyelinating lesion(s), n (%)						

latency, and greater sleep fragmentation.[38,39] In this study, the most effective components were found to be the subjective sleep quality and sleep latency. In PwMS with poor sleep quality, these components were again found to have the most significant impact on the sleep quality outcome. This situation shows that PwMS have difficulty falling asleep and are more sensitive to disturbances in the quality of their sleep.

Sleep disorders in PwMS may be caused by lesions in areas such as the diencephalon or brainstem that directly regulate the sleep-wake cycle of neurons.[40] However, there is limited research on this topic. Our study found no difference in sleep quality between patients with combined lesions, brainstem atrophy, cervical spinal cord atrophy, or CCI, another atrophy indicator.

Study Limitation

The PSQI provides a cross-sectional assessment. Cross-sectional studies may not be sufficient to prove causality. Therefore, factors that may affect sleep quality, such as relapse duration, comorbidities, medication use, depressive mood, and disease progression, were excluded from our study. This allowed our results to show a more realistic clinical-radiologic correlation. This study did not assess fatigue, restless legs syndrome, or sleep apnea. However, no difference in sleep quality was found between patients reporting long intervals between breaths during sleep and twitching or jerking of the legs while sleeping on the PSQI component questions. This finding suggests that these two factors are not significant for this cohort. In addition to the sleep quality index, prospective studies are needed to

Table 3. Differences in corpus callosum index, brainstem, and spinal cord atrophy measurements according to sleep quality						
Radiologic measurements		**Total**	**Good**	**Poor**	**P all**	**Correlation analysis**
Corpus callosum index		0.36 (0.06), 0.36 (0.12-0.5)	0.36 (0.07), 0.36 (0.12-0.5)	0.36 (0.06), 0.36 (0.17-0.46)	0.761	r=0.092 p=0.286
Brainstem	**Cerebral peduncle thickness, mm**	15.3 (1.35), 15.2 (12-18)	15.29 (1.38), 15.3 (12-18)	15.3 (1.29), 15.2 (12.5-18)	0.835	r=0.037 p=0.664
	Interpeduncular angle, (°)	67.73 (10.41), 69 (16-86)	67.22 (10.82), 68 (16-86)	68.82 (9.5), 70.5 (48-86)	0.409	r=0.027 p=0.756
	Middle cerebellar peduncle thickness, mm	16.63 (1.48), 17 (12-21)	16.52 (1.45), 17 (12-21)	16.87 (1.52), 17 (12-20)	0.190	r=0.127 p=0.140
	Midbrain thicness, mm	11.55 (1.57), 11 (9-17.4)	11.54 (1.65), 11 (9-17.4)	11.56 (1.39), 11.15 (10-14.8)	0.925	r=0.083 p=0.335
	Pons thickness, mm	21.88 (1.53), 22 (16-26)	21.8 (1.56), 22 (16-26)	22.04 (1.49), 22 (19-24.3)	0.334	r=0.062 p=0.473
	Medulla thickness, mm	12.45 (1.24), 12.4 (9.7-15)	12.48 (1.32), 12.4 (9.7-15)	12.40 (1.06), 12.3 (10.6-15)	0.745	r=0.052 p=0.544
	Mamillopontine distance, mm	6.68 (1.25), 6.5 (4-12)	6.76 (1.24), 7 (5-12)	6.53 (1.26), 6.2 (4-10)	0.404	r=-0.052 p=0.543
	Midbrain height, mm	12.54 (1.57), 12.6 (9-16.6)	12.63 (1.52), 13 (9-16.6)	12.35 (1.66), 12.05 (9-15)	0.327	r=-0.016 p=0.854
	Pontomesencephalic angle, (°)	50.23 (10.02), 50 (25-85)	49.72 (8.8), 50 (26-76)	51.32 (12.11), 51 (25-85)	0.438	r=0.166 p=0.052
Cervical cord diameter, mm	**C2 sagittal**	7.65 (1.1), 7.4 (5-10.5)	7.62 (1.09), 7.4 (5-10.5)	7.71 (1.11), 7.45 (6-10)	0.767	r=0.061 p=0.479
	C3 axial	12.07 (1.03), 12 (8-16)	12.05 (1.11), 12 (8-16)	12.14 (0.86), 12 (10.3-14.3)	0.450	r=0.047 p=0.586
	C3 sagittal	7.5 (0.7), 7.5 (6-9.2)	7.52 (0.68), 7.6 (6-9)	7.47 (0.75), 7.1 (6-9.2)	0.618	r=-0.045 p=0.607
	C7 axial	10.93 (1.02), 11 (6-14)	10.83 (1.07), 11 (6-13)	11.13 (0.88), 11 (10-14)	0.168	r=0.111 p=0.200
	C7 sagittal	6.5 (0.78), 6.25 (5-8.7)	6.48 (0.76), 6.2 (5-8.7)	6.54 (0.82), 6.3 (5-8.6)	0.717	r=-0.010 p=0.913
There was no statistically significant difference in the measurements obtained from cranial and spinal MRIs between patients with good and poor sleep quality. Additionally, no correlation was found between the measurements and the GPSQI score for all patients. Mean (SD), median (min-max)						
SD: Standard deviation, CCI: Corpus callosum index, MRI: Magnetic resonance imaging, GPSQI: Global Pittsburgh Sleep Quality Index						

evaluate changes in physical performance and other sleep parameters in PwMS. In this context, our multicenter studies lay an important foundation for generalizing our results.

Conclusion

Sleep quality is negatively affected in PwMS. This impairment appears to be associated with lower extremity physical performance, although no clear relationship was observed with lesion location, atrophy, or cognitive status in the early stages of the disease. Among the PSQI subcomponents, subjective sleep quality and sleep latency emerged as the main determinants of poor outcomes, possibly reflecting patients' heightened sensitivity to their own perception of sleep quality. These findings underscore the importance of routinely evaluating sleep quality during clinical follow-up of PwMS. Furthermore, interventions specifically targeting sleep latency may hold therapeutic potential in this population. From a clinical standpoint, systematic assessment and timely management of sleep disturbances should be regarded as integral components of MS care. Addressing sleep-related problems has the potential to improve quality of life and preserve mobility and functional independence. In this context, even relatively simple interventions such as sleep hygiene counseling or non-pharmacologic strategies may serve as valuable adjuncts to conventional treatment approaches.

Finally, it should be noted that the PSQI is a cross-sectional, self-reported tool reflecting the preceding month. Prospective longitudinal studies employing objective methods such as actigraphy or polysomnography are warranted to strengthen clinical–radiologic correlations, while still accounting for patient-reported outcomes.

Ethics

Ethics Committee Approval: This study was conducted with the approval of the Bursa Uludağ University Clinical Research Ethics Committee (approval number: 2025/700-11/10, date: 11.06.2025).
Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: F.S., A.B.D., Design: F.S., B.H., A.B.D., Data Collection or Processing: F.S., F.H., R.Ö., S.N.M., A.D., Analysis or Interpretation: F.S., R.Ö., Y.D., E.O.A., A.D., E.R.K., B.H., Literature Search: F.S., F.H., R.Ö., Y.D., E.O.A., S.N.M., E.R.K., A.B.D., Writing: F.S., Y.D., E.O.A., A.B.D.

Conflict of Interest: No conflict of interest was declared by the authors.
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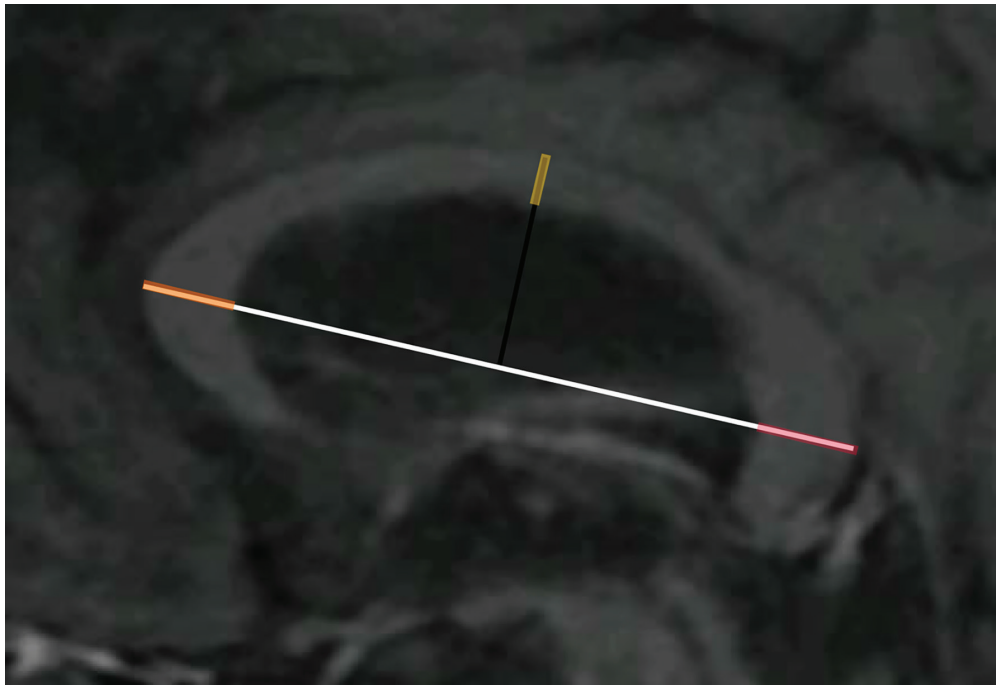
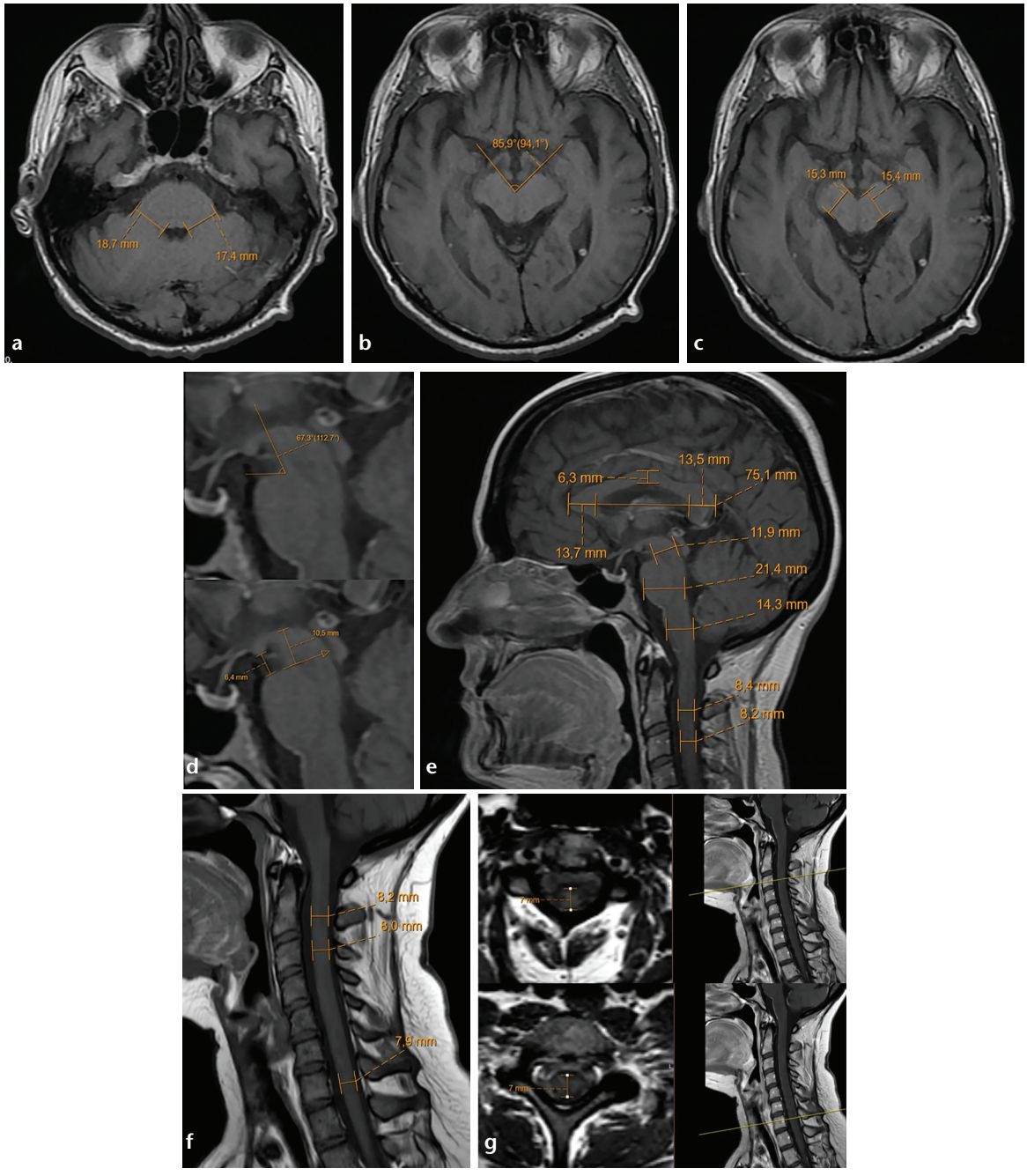


Appendix 1. Corpus callosum index measurement method: Using a simple orthogonal semi-automated system, a straight line (white-opaque) was obtained on the conventional best mid-sagittal T1W image with the largest anteroposterior diameter of the corpus callosum and a perpendicular drawn on the midline. It was normalized to the anterior (aa, orange-translucent), middle (cc, yellow-translucent), posterior (bb, red-translucent), and anteroposterior diameter (ab, white-opaque) of the corpus callosum (anterior + middle + posterior)/anteroposterior diameter; (aa + cc + bb) / ab).
For more information, see doi: 10.1016/j.mjafi.2022.06.002 and doi:10.36516/jocass.1109857



Appendix 2. Brain stem and spinal cord measurement methods: a: mid-cerebellar peduncle transverse thickness; the maximum thickness of each middle cerebellar peduncle perpendicular to its long axis was noted on both sides. b: interpeduncular angle formed between the cerebral peduncles. c: cerebral peduncle transverse thickness; the maximum thickness of the cerebral peduncle perpendicular to its long axis was noted on both sides. d: Pontomesencephalic angle; angle between the anterior surface of the midbrain and posterosuperior surface of pons at the pontomesencephalic junction (67.3°). Mamillopontine distance: distance from the inferior surface of the mammillary body to the highest point of convexity of the superior surface of the pons (6.4 mm). Midbrain height: maximum height from the ponto-mesencephalic junction level up to the midbrain roof (10.5 mm). e: Corpus callosum index measurements (13.7+6.3+13.5)/75.1 mm, see Appendix 1. Ventral midbrain anteroposterior thickness; the maximum thickness of the ventral midbrain was measured from the anterior surface up to the anterior wall of the aqueduct perpendicular to its long axis (11.9 mm). Pontine anteroposterior thickness (21.4 mm). Medullary anteroposterior thickness; the maximum thickness of the medulla was measured at its midpoint (14.3 mm). f: C2, C3, and C7 spinal cord anteroposterior sagittal diameter (C2T-S, C3T-S, C7T-S) (8.2, 8, 7.9 mm). g: C3 and C7 spinal cord anteroposterior axial diameter (C3T-A, C7T-A) (7.7 mm)