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## The impact of sleep quality on cognitive function in patients with multiple sclerosis

Cognitive impairments (CI) affect 30—70 % of patients with multiple sclerosis (MS) and can occur even in the absence of other deficits. CI are among the most debilitating manifestations, significantly impacting patients' quality of life, hindering their social activity and employment. The potential role of sleep disturbances in cognitive functioning in patients with MS is considered, with attention to the role of the glymphatic system and its activity during sleep.

**Objective** — to evaluate how sleep quality relates to the cognitive performance in patients with MS.

**Materials and methods.** The study included 32 patients with MS in the relapse phase who were not receiving disease-modifying therapy. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA), while sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI). Statistical analyses were conducted using Jamovi (version 2.3.28). Mann—Whitney U test and Spearman correlation analysis were employed, with  $p < 0.05$  considered statistically significant.

**Results.** Decreased attention, concentration, and working memory were significantly correlated with later sleep onset and the presence of sleep disturbances. The short-term memory domain showed a significant negative correlation with sleep onset latency, sleep duration, and sleep efficiency. Spearman analysis revealed a significant negative correlation between PSQI total score and MoCA total score, as well as attention, concentration, working memory, and short-term memory domains.

**Conclusions.** A moderate negative correlation exists between sleep quality scores and cognitive function, suggesting that poorer sleep may be associated with reduced cognitive function in patients with MS.

**Keywords:** multiple sclerosis, cognitive impairment, sleep quality, glymphatic system.

Multiple sclerosis (MS) is a chronic inflammatory neurodegenerative disease and a leading cause of severe disability in young adults [14]. MS has a wide range of manifestations which depend on the loci of demyelination lesions in the central nervous system (CNS) and include sensory, motor, visual disturbances, balance disorders, pelvic organ dysfunction, as well as cognitive and emotional impairments. Cognitive impairments (CI) affect 30—70 % of patients with MS and can occur even in the absence of other deficits. CI are among the most debilitating manifestations of MS, significantly impacting patients' quality of life, hindering their social activity and employment [8, 11]. Disease-related unemployment can result in social and psychological consequences,

such as depression, loneliness, anxiety, restricted community participation, and persistent stress [13].

In 2018, a systematic review assessed the relationship between employment status and CI in patients with MS. The findings demonstrated that CI led to difficulties with employment and reduced working hours [7]. According to the Atlas of MS, the global prevalence of MS is estimated to range from 20 to 300 per 100,000 people, affecting almost 3 million individuals worldwide. Regular evaluation of cognitive function in patients with MS is crucial to detect changes and initiate timely interventions. Assessment includes evaluating information processing speed, episodic memory, language, and visuospatial skills [13].

The relationship between brain atrophy and cognitive deficits in MS remains unclear. Clinical observations show instances where CI precedes the detection of cortical atrophy on neuroimaging. Conversely, early cortical atrophy may develop without noticeable CI. However, most cases demonstrate an association between gray matter atrophy and cognitive decline [2].

In 2012, two-photon in vivo imaging revealed the flow of cerebrospinal fluid (CSF) through the brain's interstitial space. This system, reliant on glial water transport and waste clearance akin to lymphatic systems, was termed the glymphatic system (GS). In rodent studies, brain clearance of soluble metabolites via the GS involved: (1) CSF flow from basal cisterns to the subarachnoid space and perivascular areas; (2) CSF entry into interstitial fluid (ISF) spaces mediated by aquaporin-4 (AQP4) water channels in astrocytes; (3) transport of the CSF-ISF-metabolite complex to perivenous spaces, exiting through lymphatic vessels and systemic circulation [9, 10]. Dysfunction of the GS is linked to aging and neurodegenerative diseases [12, 17]. Studies have shown that GS function declines due to astrocytic gliosis, AQP4 polarization loss, and reduced clearance of amyloid-beta and other metabolites in Alzheimer's disease [12, 20]. Reduced perivascular localization of AQP4 was observed in the frontal cortical gray matter in patients with CI in comparison to subjects without. Similarly, the analysis of diffusion along perivascular space index in patients with MS and healthy controls displayed an overall glymphatic impairment in first ones, with more severe affection in primary progressive MS. The reduced glymphatic fluid flow in the perivenous spaces may cause the accumulation of neuroinflammatory triggers in the white matter, thus leading to demyelinating processes [6]. Considering the abovementioned, the GS dysfunction might be involved into the pathogenesis of CI in both neurodegenerative and neuroinflammatory disorders. Recent studies revealed that amyloid-beta accumulates in the brain of healthy individuals after a single night of sleep deprivation, suggesting the GS dysfunction being a result of decreased sleep quality [18]. Given these findings, we hypothesized a potential relationship between sleep quality and CI in patients with MS.

**Objective** — to evaluate how sleep quality relates to the cognitive performance in patients with MS.

## Materials and methods

### Data

The study included 32 patients with MS without disease-modifying therapy experiencing exacerbations, treated at a tertiary care facility in Odesa, Ukraine. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA), while sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI). Data collected included patients' sex, age, MoCA total

scores, and subscores for memory, visuospatial skills, executive function, attention, language, and orientation, as well as PSQI total scores and components (e.g., sleep quality, sleep duration, disturbances).

### Outcome Assessment

MoCA is a widely accepted tool for assessing CI in MS, covering domains such as memory, executive function, attention, and language. A score of  $\leq 25$  was used to classify CI [16]. PSQI, a subjective measure of sleep quality over the past month, comprises seven components scored up to 3 points each, with higher scores indicating worse sleep quality [15].

### Statistical Analysis

Statistical analyses were conducted using Jamovi (version 2.3.28). Mann—Whitney U test and Spearman correlation analysis were employed, with  $p < 0.05$  considered statistically significant.

## Results

### Population Characteristics

The study included 20 women (mean age  $34.8 \pm 7.36$ ) and 12 men (mean age  $34.6 \pm 10.9$ ). Mann—Whitney U revealed that sex influenced executive function ( $p = 0.013$ ), but other cognitive and sleep quality measures showed no significant sex differences ( $p > 0.05$ ). Patients were divided into two groups: (1) normal cognitive function ( $n = 16$ ); (2) cognitive deficit ( $n = 16$ ) (Table 1).

Table 1  
Mann—Whitney U test results for MoCA and PSQI parameters between sex groups (male/female)

	Mann—Whitney U	p-value
MoCA total score	105.5	0.581
Visuospatial abilities	106.0	0.571
Executive functions	59.5	0.013
Attention, concentration and working memory	116.0	0.868
Language	108.0	0.605
Short term memory	91.5	0.264
Orientation to time and place	94.5	0.090
Sleep quality	114.0	0.816
Falling asleep time	112.0	0.762
Sleep duration	98.5	0.378
Sleep efficiency	119.5	1.000
Sleep disturbance	117.0	0.914
Hypnotic use	98.5	0.230
Daytime disfunction	105.5	0.570
PSQI Total Score	120.0	1.000

Note.  $H_a \mu M \neq \mu F$

**Table 2**  
Mann—Whitney U test results for MoCA parameters across groups with and without CI

	Mann—Whitney U	p-value
MoCA total score	0.0	< 0.001
Visuospatial abilities	103.0	0.160
Executive functions	87.0	0.051
Attention, concentration and working memory	74.0	0.007
Language	114.0	0.279
Short term memory	41.0	< 0.001
Orientation to time and place	127.0	0.487

Note.  $H_a \mu_1 > \mu_2$ .

*MoCA parameters across groups*

MoCA total scores, executive functions, short term memory, attention, concentration, and working memory were significantly lower in the CI group compared to the normal cognitive function group ( $p < 0.05$ ). No significant differences were observed for visuospatial skills, language, or orientation ( $p > 0.05$ ), (Table 2).

*PSQI Parameters Across Groups*

PSQI total score, falling asleep time, sleep duration and sleep efficiency were significantly higher in the group with CI ( $p < 0.05$ ). Other PSQI individual components did not showed differences between the two groups ( $p > 0.05$ ), (Table 3).

*PSQI and MoCA Correlation*

Spearman test showed significant negative correlation between PSQI total score and MoCA total score (Spearman’s rho = -0.392, df = 30,  $p = 0.013$ ), attention concentration and working memory (Spearman’s rho = -0.381, df = 30,  $p = 0.016$ ) as well as short memory components (Spearman’s rho = -0.414, df = 30,  $p = 0.009$ ).

Attention, concentration and working memory decline significantly correlated with later falling asleep time (Spearman’s rho = -0.332, df = 30,  $p = 0.032$ ) and existence of sleep disturbances (Spearman’s rho = -0.431, df = 30,  $p = 0.007$ ).

Short term memory component has a significant negative correlation with falling asleep time (Spearman’s rho = -0.474, df = 30,  $p = 0.03$ ), sleep duration (Spearman’s rho = -0.371, df = 30,  $p = 0.018$ ) and sleep efficiency (Spearman’s rho = -0.306, df = 30,  $p = 0.044$ ). The results are presented in Figure.

**Discussion**

Our study aimed to investigate the potential relationship between sleep quality and CI in patients with MS. To evaluate cognitive function, we used the MoCA

**Table 3**  
Mann—Whitney U test results for PSQI parameters across groups with and without CI

	Mann—Whitney U	p-value
Sleep quality	112.0	0.262
Falling asleep time	62.0	0.005
Sleep duration	44.5	< .001
Sleep efficiency	75.5	0.014
Sleep disturbance	95.0	0.087
Hypnotic use	114.0	0.789
Daytime disfunction	123.0	0.430
PSQI Total Score	61.5	0.006

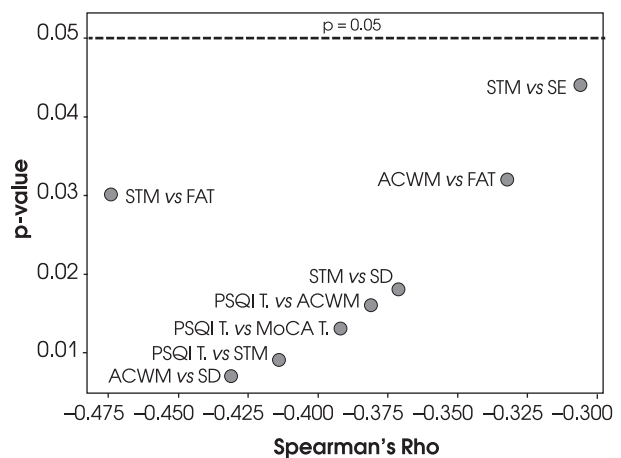
Note.  $H_a \mu_1 < \mu_2$ .

scale, where a score of  $\leq 25$  indicated CI. Sleep quality was assessed using the PSQI, with higher scores reflecting poorer sleep quality.

Based on the previously mentioned results, it can be hypothesized that there is a weak to moderate negative correlation between sleep quality and cognitive performance in patients with MS, given that the GS is primarily active during sleep.

The GS is especially active during slow-wave sleep. This activity is associated with a decrease in norepinephrine levels during sleep, leading to a significant increase in interstitial space. Conversely, during wakefulness, CSF flow and the clearance of soluble metabolites are inhibited due to high norepinephrine levels, which reduce interstitial space volume [1].

A study found that nurses who worked night shifts for over 20 years had an 80 % higher risk of developing MS compared to those who worked daytime shifts



**Fig. 1.** Spearman correlation between PSQI and MoCA parameters

Note. PSQI T. — Pittsburgh Sleep Quality Index total score; MoCA T. — Montreal Cognitive Assessment total score; STM — short term memory; SD — sleep duration; ACWM — attention, concentration and working memory; SE — sleep efficiency; FAT — falling asleep time.

[16]. Disruption of the circadian rhythm, which triggers the release of cellular and molecular inflammatory mediators, potentially leading to neuroimmune dysregulation, was proposed as a possible cause of this increased risk. Sleep disturbances affect the expression of genes involved in the synthesis and maintenance of myelin proteins. Additionally, sleep problems reduce the expression of genes necessary for the differentiation of oligodendrocyte precursor cells, which are essential for forming new myelin components in both healthy and damaged brains. Evidence also suggests that sleep disorders increase the expression of apoptotic genes and those responsible for cellular stress, which hinders nerve regeneration in MS [3].

E. Shokri-Kojori et al. studied the effects of a single night of sleep deprivation on the clearance of A $\beta$  in the human brain using PET scans. They found that one night of sleep loss significantly increased A $\beta$  burden in the right hippocampus and thalamus, areas critical for cognitive function [19].

*There is no conflict of interest.*

*Authors' participation: conception and design of the study, critical revising final approval — Yu.O. Solodovnikova; acquisition of data, analysis and interpretation of data, drafting the article — E.V. Babych, A.P. Revurko.*

*Ethics Approval. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Odesa National Medical University (protocol No. 3, dated March 12, 2025).*

*Patient Consent. Informed patient consent was waived by the Ethics Committee of Odesa National Medical University due to the retrospective nature of the study.*

L. Buratti et al. examined the relationship between sleep quality and clinical manifestations of MS. Patients with relapsing-remitting MS and a PSQI score  $\geq 5$  in the past month showed a significantly higher likelihood of adverse disease outcomes, including longer and more frequent relapses. This supports the hypothesis that poor sleep quality may impair the ability to recover from MS relapses, possibly due to defects in myelin regeneration [4].

The correlation between attention, concentration and working memory components and sleep duration was found to be the strongest one and therefore might be a subject of future research.

Our study has its limitations in the form of a small group of participants and subjectivity of PSQI results.

## Conclusions

A moderate negative correlation exists between sleep quality scores and cognitive performance, suggesting that poorer sleep may be associated with reduced cognitive function in patients with MS.

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## Вплив якості сну на когнітивну функцію пацієнтів із розсіяним склерозом

Когнітивні порушення (КП) виявляють у 30—70 % пацієнтів із розсіяним склерозом (РС). Вони можуть виникати навіть за відсутності інших клінічних дефіцитів. Когнітивні порушення є одними з виявів, які найбільш інвалідизують, що суттєво впливає на якість життя пацієнтів, перешкоджаючи їхній соціальній активності й працевлаштуванню. Розглянуто ймовірну роль розладів сну в когнітивному функціонуванні пацієнтів із РС з урахуванням ролі глімфатичної системи та її активності під час сну.

**Мета роботи** — оцінити вплив якості сну на когнітивну функцію у пацієнтів із РС.

**Матеріали та методи.** У дослідження було залучено 32 пацієнтів із РС у фазі загострення, які не отримували хворобомодифікаційну терапію. Когнітивні функції оцінювали за допомогою Монреальської когнітивної шкали (MoCA), а якість сну — за допомогою Піттсбурзького індексу якості сну (PSQI). Статистичний аналіз проводили з використанням програми Jamovi (версія 2.3.28). Застосовували U-критерій Манна—Вітні та кореляційний аналіз Спірмена. Значення  $p < 0,05$  вважали статистично значущим.

**Результати.** Загальний бал за MoCA, показники виконавчих функцій, короткочасної пам'яті, уваги, концентрації та робочої пам'яті були значно нижчими у групі з КП порівняно з групою з нормальною когнітивною функцією. Зниження уваги, концентрації та робочої пам'яті корелювало з пізнішим часом засинання й наявністю розладів сну. Домен короткочасної пам'яті мав значущу негативну кореляцію з часом засинання, тривалістю та ефективністю сну. Тест Спірмена виявив значущий негативний зв'язок між PSQI та загальним балом за MoCA, компонентами уваги, концентрації, робочої та короткочасної пам'яті.

**Висновки.** Існує помірна негативна кореляція між показниками якості сну та когнітивною діяльністю, що свідчить про те, що погіршення сну може бути пов'язане зі зниженням когнітивних функцій у пацієнтів із РС.

**Ключові слова:** розсіяний склероз, когнітивні порушення, якість сну, глімфатична система.

### ДЛЯ ЦИТУВАННЯ

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Revurko AP, Babych EV, Solodovnikova YuO. The impact of sleep quality on cognitive function in patients with multiple sclerosis. *Ukrainian Neurological Journal*. 2026;1:34-38. <http://doi.org/10.30978/UNJ2026-1-34>.