



Sleep and neuroimmunology: a narrative review

Jin Myoung Seok, Kwang Ik Yang

Sleep Disorders Center, Department of Neurology, Soonchunhyang University Hospital Cheonan, Soonchunhyang University College of Medicine, Cheonan, Korea

Numerous neuroimmunological disorders present with sleep-related symptoms. The identification of novel autoantibodies introduces new clinical categories in autoimmune diseases of the central nervous system and generates interest in the dynamic interaction between sleep and the immune system. In this review, the complex relationship among sleep, immune regulation, and neuroimmunological disorders was examined with emphasis on the vital role of sleep in modulating immune function and its influence on these conditions. This relationship emphasizes the importance of assessments and management of sleep quality in the treatment approaches for neuroimmunological disorders.

Keywords: Sleep, Neuroimmune interaction, Circadian rhythm, Neurologic autoimmune disease

Introduction

Sleep is a fundamental, recurrent behavior exhibiting a physiological state of rest and reduced consciousness [1]. Sleep homeostasis is tightly regulated by complex circadian systems that show roughly a 24-hour pattern in the regular cycle of sleep and wakefulness [2,3]. Sleep plays a crucial role in health, affecting both the nervous system and immune function [4]. Sleep and the immune system are interconnected through the effects of circadian systems on immune functions via the neuroendocrine and sympathetic systems. The immune system responds to such signals by releasing cytokines that influence sleep and circadian mechanisms [5,6]. In addition to understanding the basic physiology of sleep and its connection to the immune system, the recent discovery of novel autoantibodies in neuroimmunological disorders has generated additional interest in the relationship between sleep and neuroimmunological disorders [7-10]. The identification of novel autoantibodies targeting aquaporin-4 (AQP-4), *N*-methyl-D-aspartic acid receptor (NMDAR), and leu-

cine-rich glioma-inactivated 1 (LGI1) in conditions such as neuromyelitis optica spectrum disorders (NMOSDs) and autoimmune encephalitis has greatly enhanced the understanding of these disorders [10,11]. Patients with these conditions may experience various symptoms in addition to neurologic impairments including sleep disturbances, fatigue, and depression. These symptoms can significantly affect the quality of life [7,12,13]. Due to the interrelated nature of sleep, fatigue, and depression coupled with their relationships to neuroimmune mechanisms [12-16], understanding the association between neuroimmunological processes and sleep provides fundamental knowledge for determining their intricate connections.

The purpose of this review is to understand the complex interplay between sleep and the immune systems and to explore the clinical implications of sleep in neuroimmunological disorders.

Received: March 15, 2024 Revised: May 21, 2024 Accepted: June 2, 2024 Published online: June 25, 2024

Correspondence: Kwang Ik Yang

Sleep Disorders Center, Department of Neurology, Soonchunhyang University Hospital Cheonan, Soonchunhyang University College of Medicine, 31 Soonchunhyang 6-gil, Dongnam-gu, Cheonan 31151, Korea

E-mail: neurofan@schmc.ac.kr

ORCID: <https://orcid.org/0000-0001-6343-6520>

© 2024 by The Korean Encephalitis and Neuroinflammation Society

This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Sleep and immune system interactions

Physiology of interactions between sleep and the immune system

Sleep initiation and control are mediated by complex networks involving hypothalamic brain regions, the arousal system, and the circadian system [17]. The sleep and circadian systems modulate immune responses through neuroendocrine and sympathetic pathways, and the immune system influences these processes through cytokines [3,18]. Growth hormone and prolactin levels peak at night, even in the absence of sleep; however, these peaks can be further enhanced by sleep. Prolactin can play an immunomodulatory role through cytokine receptor modulation, and growth hormones can stimulate the proliferation of T/B cells and the synthesis of immunoglobulins [19,20]. Conversely, cortisol and catecholamines undergo suppression during sleep and are controlled by the activity of the hypothalamus-pituitary-adrenal axis and the sympathetic nervous system, respectively [21,22]. These stress hormones are the key mediators of the connection between sleep and the immune system. Dimitrov et al. [23] showed that circadian rhythms are differentially regulated by cortisol and epinephrine levels based on the number of circulating T cells. Naïve T cell subsets exhibit a negative correlation with cortisol rhythms, peaking during the night, and effector CD8+ T cell counts are positively correlated with epinephrine rhythms, reaching peak levels during the daytime (Table 1). Increases in cortisol during the daytime can cause an increase in CXCR4 expression, which can facilitate the redistribution of naïve T cells to the bone marrow. Daytime elevations in catecholamines may attenuate CD11a/CX3CR1-mediated attachment to the endothelium, potentially promoting the mobilization of effector CD8+ T cells from the marginal pool [23,24]. The circulating natural killer (NK) cell count also peaks in the early morning and is low at night and

mediated through CD11a/CX3CR1 signaling [25]. Therefore, during sleep, early-stage immune cells likely circulate in the blood, priming for adaptive immune responses, while cytotoxic effector functions dominate during wakefulness [18].

Cytokine activities exhibit circadian rhythms under neuroendocrine control [3,26,27]. Key proinflammatory cytokines such as interleukin (IL)-6, IL-12, tumor necrosis factor alpha (TNF-α), and interferon gamma typically reach their peak levels at night [26–29]. In contrast, the anti-inflammatory cytokine IL-10 shows sleep-dependent fluctuations, peaking during the daytime. Although these patterns were observed in most studies, discrepancies in IL-6 and IL-10 behavior have been reported [27,30]. Cytokines also can play an important role in sleep regulation; IL-1 and TNF-α were observed to enhance non-REM sleep, while their inhibition can suppress spontaneous sleep [31].

Sleep deprivation and immune function

The intricate interactions among the sleep/circadian system, immune cells, and cytokines are significantly altered by periods of sleep deprivation, which can introduce substantial stress that adversely affects health and immune function [18,32]. Prolonged sleep deprivation has been associated with increased proinflammatory activity, similar to that observed in chronic sleep disturbances. Notable elevations in inflammatory markers such as IL-6, TNF-α, and C-reactive protein have been observed following sleep deprivation [33]. Furthermore, sleep deprivation can lead to decreased cytotoxic activities in T cells and NK cells along with a reduction of T cell proliferative capacity [34,35]. Research on monocytes shows that sleep loss induces a functional alteration of the monocyte proinflammatory cytokine response [36]. In a previous study, acute sleep deprivation was shown to elevate anti-inflammatory cytokine IL-10 level but to have little effect on the ratio of TNF-α/

Table 1 Variations of immune cells and cytokines related to sleep

Variable	During sleep	Daytime	Sleep deprivation
Naïve T cell	↑	↓	Reduced proliferative capacity
Effector cytotoxic T cell	↓	↑	Decreased counts and cytotoxic activity
Natural killer cell	↓	↑	Decreased cytotoxic activity
Monocytes	No change	No change	Decreased function of proinflammatory cytokine response
IL-6	↑	↓	Increased level
IL-10*	↓	↑	Not altered
IL-12	↑	↓	Increased level
TNF-α	↑	↓	Increased level
IFN-γ	↑	↓	Increased level

↑, increased; ↓, decreased; IL, interleukin; TNF-α, tumor necrosis factor alpha; IFN-γ, interferon gamma.

*Some studies have reported the absence of circadian variation.

IL-10 [37]. In another study that included college students with sleep insufficiency, increased IL-10 levels were observed. Additional research is required to elucidate the contradictory results for IL-10 in the context of sleep deprivation [38]. Despite the diversity in experimental designs and definitions of sleep deprivation in studies, a common finding is that sleep deprivation promotes proinflammatory activity and attenuates immune function. The variations in immune cells and cytokines associated with sleep are presented in Table 1 and Figure 1.

Clinical aspects of sleep and neuroimmunological disorders

Alteration of sleep as a risk factor for neuroimmunological disorders

Due to the relationship between sleep and the immune system and the effects of sleep deprivation on immune function, alterations in sleep can be considered a risk factor for neuroimmunological disorders. This connection is well documented in studies on multiple sclerosis (MS). An association between shift work and subsequent risk of MS has been established; starting shift work before 20 years of age was found to significantly increase MS risk [39]. Other studies in which nurse cohorts were included, a history of night shift work spanning 20 years or more was associated with increased risk of MS [40]. Therefore, beginning shift work at a younger age appears to significantly influence the association between

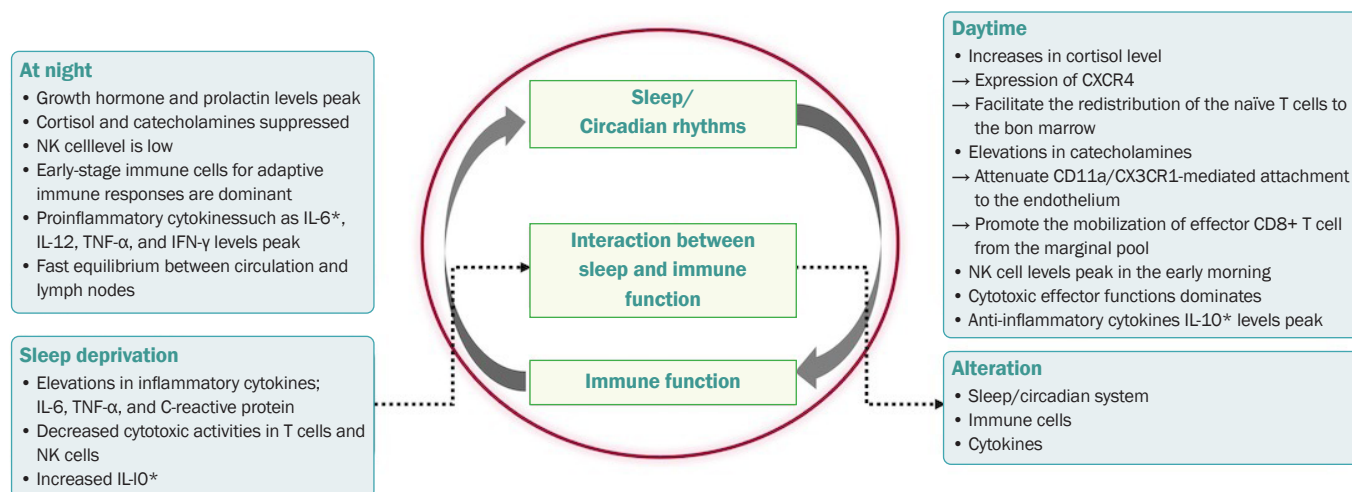
shift work and MS risk. Furthermore, research conducted in Sweden on sleep patterns and risk of MS in adolescence revealed that insufficient sleep and poor sleep quality during adolescence increased the risk of MS in a dose-dependent manner [41]. Thus, adequate sleep at a young age, essential for proper immune function, could be a preventive factor against MS [41].

Sleep loss is associated with the disease activity of many autoimmune conditions, including systemic lupus erythematosus, Sjögren disease, and inflammatory bowel disease [42–44]. Similarly, the outcome of MS is associated with sleep quality; poor sleep quality negatively affects MS outcomes by possibly influencing the efficiency of remyelination processes [45]. In a previous study, sleep disturbance was indicated as a possible trigger for acute MS exacerbation [46]. Sleep should be regarded as an important clinical factor when evaluating the disease activity of neuroimmunological disorders.

Sleep-related clinical features of neuroimmunological disorders

The influence of sleep disturbance on immune regulation is bidirectional, as imbalances in the immune system can contribute to sleep disruptions. Central nervous system (CNS) demyelinating disorders may result in brain lesions in sleep- and/or circadian rhythm-related brain structures, leading to symptomatic sleep disorders. Inflammation within the CNS may be directly related to sleep disturbance, and autoanti-

Figure 1 Interactions between sleep and immune function



NK, natural killer; IL, interleukin; TNF- α , tumor necrosis factor alpha; IFN- γ , interferon gamma.

*There are inconsistent reports in other studies.

bodies targeting neuronal proteins in the brain may cause sleep disorders [47].

Symptomatic narcolepsy cases consist of heterogeneous disease conditions, often involving lesions in the hypothalamus [48]. Although AQP-4 is highly expressed in hypothalamic periventricular regions, MS can present as symptomatic narcolepsy with hypothalamic lesions. NMOSD, which is associated with a disease-specific autoantibody targeting AQP-4, can frequently exhibit hypothalamic lesions accompanied by symptomatic narcolepsy [49]. Patients with MS may be at increased risk of obstructive sleep apnea, especially when they have brainstem lesions [50]. In addition, chronic insomnia is a common issue among MS patients [51]. Fatigue in MS has been the subject of extensive research due to its significant effect on patients. Evaluating sleep quality is essential for assessing fatigue and depression, which are critical factors for quality of life in MS patients [52]. Therefore, sleep evaluation should be included in a clinical assessment for MS patients. Individuals with NMOSD may experience diminished sleep quality from the early stages of the disease [13]. One study using polysomnography in NMOSD cases showed that sleep architectures in NMOSD patients are markedly disrupted [9]. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), for which diagnostic criteria have only recently been established [8], has yet to be extensively studied

in terms of sleep. Hypersomnia with hypothalamic lesions was reported in a MOGAD patient [53].

Sleep can be altered in various ways, with all types of sleep disorders potentially arising in autoimmune encephalitis. However, such sleep-related symptoms are frequently unnoticed due to the predominance of other neurological and psychiatric symptoms [7]. Insomnia associated with autoimmune encephalitis, such as anti-NMDAR, anti-Caspr2, and anti-LGI1 encephalitis, is typically acute and severe, often accompanied by hallucinations or abnormal behaviors [54,55]. In patients with anti-NMDAR encephalitis, the disease typically progresses through two main clinical phases: acute and recovery. Sleep disturbances also follow this pattern, with insomnia commonly occurring in the early acute stage and later being replaced by hypersomnia. This transition between clinical phases is closely associated with decreased NMDAR levels, followed by a gradual restoration of NMDAR function. Therefore, NMDAR function plays a key role in the occurrence of insomnia and the subsequent hypersomnia in anti-NMDAR encephalitis [56].

Anti-immunoglobulin-like cell adhesion molecule 5 (IgLON5) disease is characterized by complex sleep disorders. Due to the rarity and gradual progression of this condition, such sleep disturbances may be a key indicator for diagnosis. Ap-

Table 2 Clinical characteristics of sleep alteration in neuroimmunological disorders

Disorder	Autoantibody	Associated brain lesion	Clinical features
Multiple sclerosis	None	Hypothalamic lesion	Symptomatic narcolepsy Poor sleep quality Insomnia
NMOSD	Anti-aquaporin4 Ab	Hypothalamic lesion	Symptomatic narcolepsy Poor sleep quality
MOGAD Autoimmune encephalitis	Anti-MOG Ab	Hypothalamic lesion	Hypersomnia
	Anti-NMDAR Ab	Reticular activating system	Insomnia Hypersomnia
	Anti-LGI1-Ab	Reticular activating system Thalamic/hypothalamic lesion	Insomnia Hypersomnolence
		Limbic system	RBD
	Anti-Caspr2 Ab	Reticular activating system	Insomnia Morvan syndrome
	Anti-IgLON5 Ab	Medulla neuronal loss*	Insomnia RBD OSA Non-REM parasomnia
	Anti-Hu Ab	Brainstem neuronal loss*	Central hypoventilation
	Anti-Ma2 Ab	Loss of hypothalamic neurons*	Symptomatic narcolepsy

Ab, antibody; NMOSD, neuromyelitis optica spectrum disorders; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; NMDAR, N-methyl-D-aspartic acid receptor; LGI1, leucine-rich glioma-inactivated 1; RBD, REM sleep behavior disorder; OSA, obstructive sleep apnea.

*Reported in autopsy studies.

proximately 70% of patients experience insomnia with excessive daytime sleepiness. Laryngeal stridor and unusual behaviors during sleep can be identified [7,57]. In addition, REM sleep behavior disorder is frequently observed, with prominent limb and body jerks. The precise pathomechanisms of anti-IgLON5 disease and its associated sleep disturbances remain unclear. However, some studies have shown that sleep abnormalities in anti-IgLON5 diseases can be modified or normalized after immune therapies, indicating a relationship between the immune system and sleep abnormalities in this disease [57]. Further studies are needed to clarify the pathophysiology of sleep disturbance in anti-IgLON5 disease. Other types of sleep manifestations in neuroimmunological disorders are presented in Table 2 [58].

It is crucial to recognize that drugs used to treat these neuroimmunological disorders can impact sleep. For example, steroids can cause insomnia, neuroleptics can lead to hypersomnolence, and certain benzodiazepines may induce abnormal behaviors during sleep. These side effects of treatment are common in clinical practice and should be considered in the management of affected patients.

Conclusion

This review has highlighted the complex interconnection between sleep, the immune system, and neuroimmunological disease. Immune cells and cytokines have circadian variations. Notably, inadequate sleep and sleep deprivation can disrupt these rhythms and are potential contributors to the onset and worsening of neuroimmunological disorders. Sleep and neuroimmunological diseases have a two-way relationship, and neuroimmunological diseases can cause sleep disorders. By integrating sleep management into the therapeutic strategy for these conditions, clinicians can offer more targeted and effective treatments, ultimately improving outcomes and quality of life for patients with neuroimmunological diseases.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Conceptualization: all authors; Supervision: Yang KI; Writing-original draft: JM Seok; Writing-review & editing: all authors.

References

1. Sejnowski TJ, Destexhe A. Why do we sleep? *Brain Res* 2000;886:208–223.
2. Foster RG. Sleep, circadian rhythms and health. *Interface Focus* 2020;10:20190098.
3. Lange T, Dimitrov S, Born J. Effects of sleep and circadian rhythm on the human immune system. *Ann N Y Acad Sci* 2010;1193:48–59.
4. Bryant PA, Trinder J, Curtis N. Sick and tired: does sleep have a vital role in the immune system? *Nat Rev Immunol* 2004;4:457–467.
5. Coogan AN, Wyse CA. Neuroimmunology of the circadian clock. *Brain Res* 2008;1232:104–112.
6. Imeri L, Opp MR. How (and why) the immune system makes us sleep. *Nat Rev Neurosci* 2009;10:199–210.
7. Muñoz-Lopetegui A, Graus F, Dalmau J, Santamaria J. Sleep disorders in autoimmune encephalitis. *Lancet Neurol* 2020;19:1010–1022.
8. Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. *Lancet Neurol* 2023;22:268–282.
9. Song Y, Pan L, Fu Y, et al. Sleep abnormality in neuromyelitis optica spectrum disorder. *Neurol Neuroimmunol Neuroinflamm* 2015; 2:e94.
10. Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol* 2016;15:391–404.
11. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2015;85:177–189.
12. Kaminska M, Kimoff RJ, Schwartzman K, Trojan DA. Sleep disorders and fatigue in multiple sclerosis: evidence for association and interaction. *J Neurol Sci* 2011;302:7–13.
13. Seok JM, Choi M, Cho EB, et al. Fatigue in patients with neuromyelitis optica spectrum disorder and its impact on quality of life. *PLoS One* 2017;12:e0177230.
14. Dantzer R, Heijnen CJ, Kavelaars A, Laye S, Capuron L. The neuroimmune basis of fatigue. *Trends Neurosci* 2014;37:39–46.
15. Irwin MR, Olmstead R, Carrillo C, et al. Sleep loss exacerbates fatigue, depression, and pain in rheumatoid arthritis. *Sleep* 2012;35:537–543.
16. Lavidor M, Weller A, Babkoff H. How sleep is related to fatigue. *Br J Health Psychol* 2003;8(Pt 1):95–105.
17. Carley DW, Farabi SS. Physiology of sleep. *Diabetes Spectr* 2016;29:5–9.
18. Besedovsky L, Lange T, Born J. Sleep and immune function. *Pflugers Arch* 2012;463:121–137.
19. Meazza C, Pagani S, Travaglini P, Bozzola M. Effect of growth hormone (GH) on the immune system. *Pediatr Endocrinol Rev* 2004;1 Suppl 3:490–495.
20. Rasmi Y, Jalali L, Khalid S, et al. The effects of prolactin on the immune system, its relationship with the severity of COVID-19, and its

- potential immunomodulatory therapeutic effect. *Cytokine* 2023; 169:156253.
21. Linsell CR, Lightman SL, Mullen PE, Brown MJ, Causon RC. Circadian rhythms of epinephrine and norepinephrine in man. *J Clin Endocrinol Metab* 1985;60:1210–1215.
 22. Follenius M, Brandenberger G, Bandesapt JJ, Libert JP, Ehrhart J. Nocturnal cortisol release in relation to sleep structure. *Sleep* 1992;15:21–27.
 23. Dimitrov S, Benedict C, Heutling D, Westermann J, Born J, Lange T. Cortisol and epinephrine control opposing circadian rhythms in T cell subsets. *Blood* 2009;113:5134–5143.
 24. Dimitrov S, Lange T, Born J. Selective mobilization of cytotoxic leukocytes by epinephrine. *J Immunol* 2010;184:503–511.
 25. Bourin P, Mansour I, Doinel C, Roué R, Rouger P, Levi F. Circadian rhythms of circulating NK cells in healthy and human immunodeficiency virus-infected men. *Chronobiol Int* 1993;10:298–305.
 26. Sothorn RB, Roitman-Johnson B, Kanabrocki EL, et al. Circadian characteristics of circulating interleukin-6 in men. *J Allergy Clin Immunol* 1995;95(5 Pt 1):1029–1035.
 27. Lange T, Dimitrov S, Fehm HL, Born J. Sleep-like concentrations of growth hormone and cortisol modulate type1 and type2 in-vitro cytokine production in human T cells. *Int Immunopharmacol* 2006; 6:216–225.
 28. Redwine L, Hauger RL, Gillin JC, Irwin M. Effects of sleep and sleep deprivation on interleukin-6, growth hormone, cortisol, and melatonin levels in humans. *J Clin Endocrinol Metab* 2000;85:3597–3603.
 29. Dimitrov S, Lange T, Benedict C, et al. Sleep enhances IL-6 trans-signaling in humans. *FASEB J* 2006;20:2174–2176.
 30. Lissoni P, Rovelli F, Brivio F, Brivio O, Fumagalli L. Circadian secretions of IL-2, IL-12, IL-6 and IL-10 in relation to the light/dark rhythm of the pineal hormone melatonin in healthy humans. *Nat Immun* 1998;16:1–5.
 31. Krueger JM, Obál FJ, Fang J, Kubota T, Taishi P. The role of cytokines in physiological sleep regulation. *Ann N Y Acad Sci* 2001;933:211–221.
 32. Dinges DE, Douglas SD, Hamarman S, Zaugg L, Kapoor S. Sleep deprivation and human immune function. *Adv Neuroimmunol* 1995;5:97–110.
 33. Meier-Ewert HK, Ridker PM, Rifai N, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *J Am Coll Cardiol* 2004;43:678–683.
 34. Bollinger T, Bollinger A, Skrum L, Dimitrov S, Lange T, Solbach W. Sleep-dependent activity of T cells and regulatory T cells. *Clin Exp Immunol* 2009;155:231–238.
 35. Irwin M, Mascovich A, Gillin JC, Willoughby R, Pike J, Smith TL. Partial sleep deprivation reduces natural killer cell activity in humans. *Psychosom Med* 1994;56:493–498.
 36. Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. *Arch Intern Med* 2006;166:1756–1762.
 37. Wright KP Jr, Drake AL, Frey DJ, et al. Influence of sleep deprivation and circadian misalignment on cortisol, inflammatory markers, and cytokine balance. *Brain Behav Immun* 2015;47:24–34.
 38. Zhai S, Tao S, Wu X, et al. Associations of sleep insufficiency and chronotype with inflammatory cytokines in college students. *Nat Sci Sleep* 2021;13:1675–1685.
 39. Hedström AK, Åkerstedt T, Olsson T, Alfredsson L. Shift work influences multiple sclerosis risk. *Mult Scler* 2015;21:1195–1199.
 40. Papantoniou K, Massa J, Devore E, et al. Rotating night shift work and risk of multiple sclerosis in the Nurses' Health Studies. *Occup Environ Med* 2019;76:733–738.
 41. Åkerstedt T, Olsson T, Alfredsson L, Hedström AK. Insufficient sleep during adolescence and risk of multiple sclerosis: results from a Swedish case-control study. *J Neurol Neurosurg Psychiatry* 2023; 94:331–336.
 42. Xerfan EM, Andersen ML, Tomimori J, Tufik S, Facina AS. The role of sleep in the activity of lupus erythematosus: an overview of this possible relationship. *Rheumatology (Oxford)* 2021;60:483–486.
 43. Parekh PJ, Oldfield IV EC, Challapallisri V, Ware JC, Johnson DA. Sleep disorders and inflammatory disease activity: chicken or the egg? *Am J Gastroenterol* 2015;110:484–488.
 44. Gudbjörnsson B, Broman JE, Hetta J, Hällgren R. Sleep disturbances in patients with primary Sjögren's syndrome. *Br J Rheumatol* 1993;32:1072–1076.
 45. Buratti L, Iacobucci DE, Viticchi G, et al. Sleep quality can influence the outcome of patients with multiple sclerosis. *Sleep Med* 2019; 58:56–60.
 46. Sahraian MA, Rezaali S, Hosseiny M, Doosti R, Tajik A, Naser Moghadas A. Sleep disorder as a triggering factor for relapse in multiple sclerosis. *Eur Neurol* 2017;77:258–261.
 47. Iranzo A. Sleep and neurological autoimmune diseases. *Neuropsychopharmacology* 2020;45:129–140.
 48. Kanbayashi T, Shimohata T, Nakashima I, et al. Symptomatic narcolepsy in patients with neuromyelitis optica and multiple sclerosis: new neurochemical and immunological implications. *Arch Neurol* 2009;66:1563–1566.
 49. Pittock SJ, Weinshenker BG, Lucchinetti CF, Wingerchuk DM, Corboy JR, Lennon VA. Neuromyelitis optica brain lesions localized at sites of high aquaporin 4 expression. *Arch Neurol* 2006;63:964–968.
 50. Braley TJ, Segal BM, Chervin RD. Sleep-disordered breathing in multiple sclerosis. *Neurology* 2012;79:929–936.
 51. Braley TJ, Segal BM, Chervin RD. Obstructive sleep apnea and fatigue in patients with multiple sclerosis. *J Clin Sleep Med* 2014;10:155–162.

52. Lobentanz IS, Asenbaum S, Vass K, et al. Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality. *Acta Neurol Scand* 2004;110:6–13.
53. Menjo K, Ashida S, Murata S, et al. MOG-antibody-associated disorder with hypothalamic lesions associated with hypersomnia and decrease of orexin in CSF: a case report. *Clin Exp Neuroimmunol* 2022;13:251–255.
54. Cornelius JR, Pittock SJ, McKeon A, et al. Sleep manifestations of voltage-gated potassium channel complex autoimmunity. *Arch Neurol* 2011;68:733–738.
55. DeSena AD, Greenberg BM, Graves D. “Light switch” mental status changes and irritable insomnia are two particularly salient features of anti-NMDA receptor antibody encephalitis. *Pediatr Neurol* 2014;51:151–153.
56. Ariño H, Muñoz-Lopetegi A, Martinez-Hernandez E, et al. Sleep disorders in anti-NMDAR encephalitis. *Neurology* 2020;95:e671–e684.
57. Gaig C, Iranzo A, Cajochen C, et al. Characterization of the sleep disorder of anti-IgLON5 disease. *Sleep* 2019;42:zsz133.
58. Blattner MS, Day GS. Sleep disturbances in patients with autoimmune encephalitis. *Curr Neurol Neurosci Rep* 2020;20:28.