Nature and Science of Sleep

Open Access Full Text Article

REVIEW

The Mechanisms of Magnesium in Sleep Disorders

Caijun He[1], Biao Wang[1], Xuanyu Chen[1], Jiacheng Xu[2], Yaxin Yang[1], Mei Yuan[1,2]

[1]Department of Neurology, Hengyang Medical School, The Second Affiliated Hospital, University of South China, Hengyang, 421001, People's Republic of China; [2]Department of Neurology, Hengyang Medical School, Affiliated Nanhua Hospital, University of South China, Hengyang, 421001, People's Republic of China

Correspondence: Mei Yuan, Department of Neurology, Hengyang Medical School, Affiliated Nanhua Hospital, University of South China, Hengyang, 421001, People's Republic of China, Email 2012020002@usc.edu.cn

Abstract: Sleep is a highly elaborate biological occurrence, necessitating the combined action and participation of diverse brain regions. The sleep-wake cycle is regulated by a multitude of factors, including various hormones produced by the hypothalamus and external stimuli. Sleep disorders can accelerate the progression of numerous diseases or directly trigger the onset of many health conditions. However, the specific regulatory mechanisms remain elusive. In recent years, the role of magnesium in sleep disorders has garnered considerable attention. Magnesium not only reduces the excitability of the nervous system and alters muscle relaxation but also regulates cellular biological clocks, energy balance, and circadian rhythms, playing a crucial role in sleep regulation. Magnesium deficiency not only shortens the effective sleep duration but also impairs sleep quality, leading to various specific sleep disorders. Additionally, magnesium supplements can improve sleep parameters in a variety of sleep-related diseases, especially those associated with the occurrence and development of sleep disorders. Therefore, a more in-depth understanding of the impact of magnesium on sleep disorders may reveal new therapeutic targets for sleep-related diseases. In this review, we comprehensively summarize the latest key findings on the mechanism of action of magnesium in sleep health and its role in initiating or exacerbating common sleep disorders, providing new insights into the diagnosis and treatment of sleep disorder-related diseases.

Keywords: magnesium, sleep, sleep disorder

Introduction

Magnesium (Mg), the second most abundant mineral in the human body, participates in over 300 biochemical reactions. Serving as an essential cofactor for numerous enzymatic reactions, it plays a pivotal role in maintaining cellular functions and physiological homeostasis.[1] Magnesium is pivotal to a wide array of biological processes, including oxidative phosphorylation, energy generation, glycolysis, and the biosynthesis of proteins and nucleic acids.[2] A large proportion of the body's magnesium is sequestered in bones and cells. The homeostasis of intracellular magnesium ions is intricately intertwined with the metabolism of other intracellular cations, notably potassium (K^+), sodium (Na^+), and calcium (Ca^{2+}), via mechanisms such as Na^+/K^+-ATPase, Ca^{2+}-activated K^+ channels, and other regulatory pathways. This interconnected ion regulation is fundamental to neural conduction within the nervous system, ensuring proper transmission of electrical signals and overall neuronal function.[3] Magnesium ions also participate in muscle contraction, control neuronal excitability, and influence neurotransmitter cycling by regulating the transmembrane transport of other ions. This role is particularly crucial in the regulation of sleep.[4]

Methods

This narrative review centers on the function of magnesium in sleep regulation, with a particular emphasis on populations affected by sleep disorders. Relevant primary research articles were retrieved using a structured search approach. Specifically, we conducted literature searches in PubMed and Web of Science, encompassing both human and animal studies. The review encompasses a broad range of topics, with key search terms including "magnesium", "Mg", "Mg^{2+}", "sleep", "sleep disorder", "sleep disorders", "sleep quality", "sleep disturbances", "sleep structure", "sleep-wake", "circadian rhythm", "insomnia", "idiopathic hypersomnia and narcolepsy", "idiopathic hypersomnia or narcolepsy", "obstructive sleep apnea", "OSA", "Restless legs syndrome/Willis-Ekbom disease", "RLS/WED", "therapeutic interventions", and "sex differences". The literature search was not restricted by publication timeline, with inclusion criteria

Received: 16 July 2025
Accepted: 11 September 2025
Published: 15 October 2025

specifying only English-language articles for analysis. After eliminating duplicate records, an initial screening was performed using titles and abstracts to identify studies that might be relevant to the research questions. The shortlisted studies then underwent a full-text review to confirm their consistency with the review' s objectives. Articles were excluded if they did not focus on sleep disorders, lacked sleep assessment components, or had inaccessible full texts. A flow diagram depicting the study selection process is presented in Figure 1. To evaluate the quality of the study, the Newcastle-Ottawa Quality Assessment Scale (NOS)[5] and the Cochrane Collaboration tool[6] was used for human studies in Table 1. Low, moderate, and high risk of bias were used as the score for evaluation.

Sleep and Sleep Disorders

Sleep is a fundamental physiological process crucial for restoring diverse psychophysiological functions. It facilitates the consolidation of learning and memory, replenishes energy expended by the central nervous system and metabolism during wakefulness, and supports the recovery of immune and endocrine systems.[19] Current guidelines recommend that adults maintain optimal health and daytime performance by achieving a minimum of 7 hours of total sleep per night with a sleep efficiency of at least 85%.[20,21] Notably, a comprehensive global survey encompassing participants aged 15–65 highlights a significant prevalence of sleep disorders. In the United States, 56% of respondents reported experiencing sleep disturbances, with 55–69% of those affected struggling with sleep initiation, 63–78% facing sleep maintenance issues, and 31–52% reporting poor overall sleep quality. Similar trends were observed in Western Europe (31%) and Japan (23%),[22] indicating that sleep disorders represent a widespread public health concern across different regions. Impairments in sleep quantity and quality can manifest as symptoms of sleep disorders, such as daytime somnolence, excessive daytime sleepiness, and nocturnal snoring. In accordance with the International Classification of Sleep Disorders, sleep disorders fall into seven primary categories: insomnia, sleep-related breathing disorders, central disorders of hypersomnolence, circadian rhythm sleep-wake

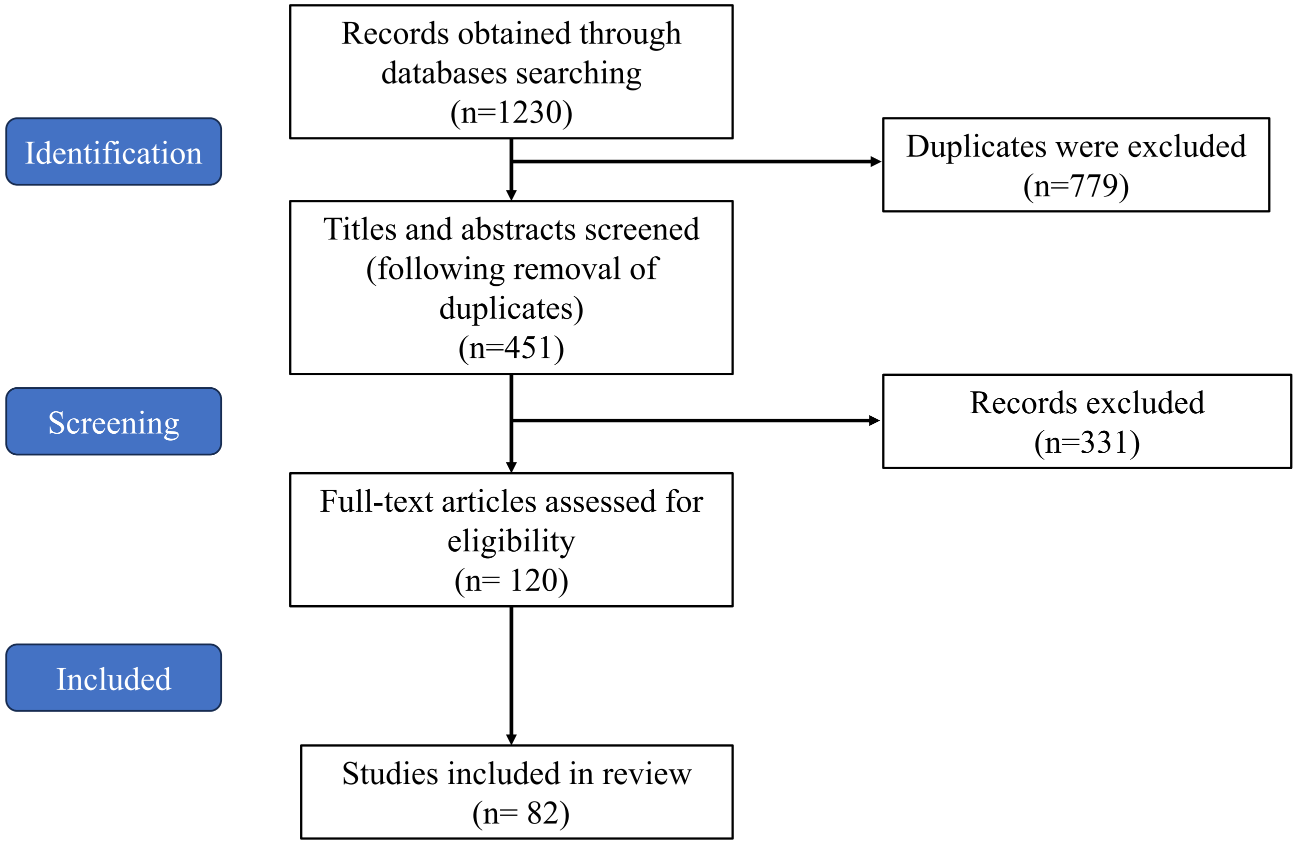

Figure 1 Flowchart of the search and selection process for included studies.

Notes: PRISMA Figure adapted from Moher D, Liberati A, Tetzlaff J et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ, 2009, 339: b2535.[7]

Table 1 Magnesium in Sleep Disorders

Study	**N**	**Sex (M/F)**	**Mean Age/Age Range**	**Duration**	**Study Design**	**Sleep Measures**	**Participant's Health Status**	**Intervention of Experimental Group**	**Intervention of Control Group**	**Outcomes**	**Limitations**	**ROB**	**Sleep Disorders**
Sato-Mito et al 2010[8]	3304	3304 F	18–20	/	CS	Self-report	Healthy	/	/	Late midpoint of sleep negatively associated with dietary intake of Mg	Sleep midpoint was determined based on bedtime and rise time recorded on weekdays, with no inclusion of free-day data	High	Insomnia
Nielsen et al 2010[9]	100	22/78	59	7 w	RCT	PSQI	Adults with sleep complaints	320 mg Mg citrate	Sodium citrate	Mg supple mentation improved overall PSQI score	Absence of the details of sleep health	Low	Insomnia
Abbasi et al 2012[10]	46	23/23	65	8 w	RCT	ISI	Elderly people experiencing primary insomnia	828 mg Mg oxide tablets (500 mg elemental)	Placebo	Supplementation of Mg appears to improve subjective and objective measures of insomnia in elderly people.	Small sample size Short duration	High	Insomnia
Tunc et al 2023[11]	938	279/659	81.1	/	R	ISI, ESS	Elderly outpatient patients	/	/	Hypomagnesemia is Associated with EDS	Unknown if EDS leads to hypomagnesemia or vice versa. It is possible that the relationship is bidirectional.	High	IH/NCL
Luo et al 2024[12]	20,585	10,149/10,436	48.8	/	CS	MDS score	Adults aged ≥20 years who participated in NHANES 2005-2014	/	/	Revealed a positive correlation between the MDS and excessive sleep, especially among non-depressed elderly individuals	Assessing excessive sleep based on sleep duration carries the risk of subjective patient bias	High	IH/NCL
Lai et al 2015[13]	98	55/43	57.12	/	CS	PSQI, ESS	Peritoneal dialysis patients	/	/	Patients experiencing excessive daytime sleepiness showed higher levels of serum Mg. Higher PSQI scores correlated positively with Mg levels.	Subjective assessment of sleep health and medications were not controlled	High	IH/NCL
Karamanli et al 2017[14]	98	60/38	47.5–52.3	1 year	R	AHI, ODI, CRP, TST	Patients with OSA or without OSA	68 patients with newly diagnosed mild to severe OSA	30 patients without OSA	Mg levels changed depending on the presence and severity of OSA. Low levels were associated with a higher CRP concentration in patients with OSA.	Small number of participants	Fair	OSA
Jiao et al 2016[15]	39	15/24	44.2–50.5	/	CS	ESS, PSG test	OSAHS patients with obesity and type 2 diabetes mellitus (T2DM) who had received RYGB surgery.	/	/	Blood Mg levels of OSA patients (n=39) increased significantly after Roux-en-Y gastric bypass (RYGB) surgery compared with pre-intervention levels	/	Low	OSA
Yildirim et al 2021[16]	253	253 F	27.25–28.10	6 month	CC	BAI, BDI, PSQI	Pregnant women	Diagnosed with RLS	Healthy pregnant women (n = 134)	Mg therapy reduced disease symptom intensity and improved patients' sleep quality	Post-natal RLS symptoms and newborn outcomes of the participants were not evaluated	High	RLS/WED

(*Continued*)

Table 1 (Continued).

Study	N	Sex (M/F)	Mean Age/Age Range	Duration	Study Design	Sleep Measures	Participant's Health Status	Intervention of Experimental Group	Intervention of Control Group	Outcomes	Limitations	ROB	Sleep Disorders
Bartel et al 2006[17]	1	1 M	34	2 days	/	Self-report	A 34-year-old gravida 1 para 0 woman, with a 13-year history of RLS	2g of MgSO4 per hour for 2 days	/	Reported that a patient with RLS/WED made a full recovery after receiving an intravenous injection of MgSO4	Small sample size	High	RLS/WED
Hornyak et al 1998[18]	10	6/4	57	4-6 w	NRCT	PSQI, ESS	Insomnia related to PLMS (n=4) or mild-to-moderate RLS (n=6)	Mg was administered orally at a dose of 12.4 mmol in the evening	/	Mg treatment may be a useful alternative therapy in patients with mild or moderate RLS- or PLMS-related insomnia	Small sample size	High	RLS/WED

Abbreviations: ROB, Risk of bias assessment; OSA, Obstructive sleep apnea; M, Male; F, Female; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale; EEG, electroencephalogram; ISI, Insomnia Severity Index; IH/NCL, Idiopathic hypersomnia and narcolepsy; RLS/WED, Restless legs syndrome/Willis-Ekbom disease; AHI, Apnea–Hypopnea Index; ODI, Oxygen desaturation index; CRP, Plasma C-reactive protein; TST, Total sleep time; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CC, Case-control; CS, Cross sectional; R, Retrospective; RCT, Parallel randomized controlled trial; NRCT, Non-randomized clinical trial; N, Sample size; Mg, Magnesium; MgSO4, Magnesium sulfate; PSG, Polysomnography; MDS, Mg Deficiency Score; EDS, Excessive Daytime Sleepiness.

disorders, sleep-related movement disorders, parasomnias, and other sleep disorders.[23] Sleep and sleep disorders are associated with multiple factors. Research analyses have indicated that middle-aged individuals, men, those with obesity, individuals with low magnesium intake, and patients with depression are more prone to sleep problems and sleep disorders.[12] This study focuses on the role of magnesium in sleep, especially among individuals with sleep disorders. This review comprehensively summarizes the mechanisms through which magnesium modulates sleep and the latest progress in its therapeutic application for sleep disorders, with the aim of offering novel perspectives for the management of sleep-related diseases.

Magnesium in Sleep

Sleep constitutes an active process requiring the coordinated engagement of multiple brain regions. The daily sleep-wake cycle is regulated by a variety of hormones synthesized in the hypothalamus, alongside external stimuli—most notably, photons of light.[24,25] Neurochemical signals—specifically neurotransmitters—govern our sleep-wake states through their actions on distinct neuronal populations within the brain. To date, a multitude of sleep-regulating substances have been identified, which can be classified into two fundamental categories: wake-promoting neurochemical factors, such as norepinephrine, serotonin, acetylcholine, histamine, and orexin; and sleep-promoting systems, including gamma-aminobutyric acid (GABA), adenosine, and nitric oxide.[24,25] Among these, magnesium exerts a critical role in the physiological regulation of sleep-modulating substances (Figure 2).

Magnesium in the Glutamatergic and GABAergic Systems

L-glutamate stands out as a vital excitatory neurotransmitter within the mammalian central nervous system. It acts by stimulating orexinergic neurons, which subsequently promotes wakefulness while inhibiting both the non-rapid eye movement (NREM) and rapid eye movement (REM) sleep stages.[27] N-methyl-D-aspartic acid (NMDA), a naturally

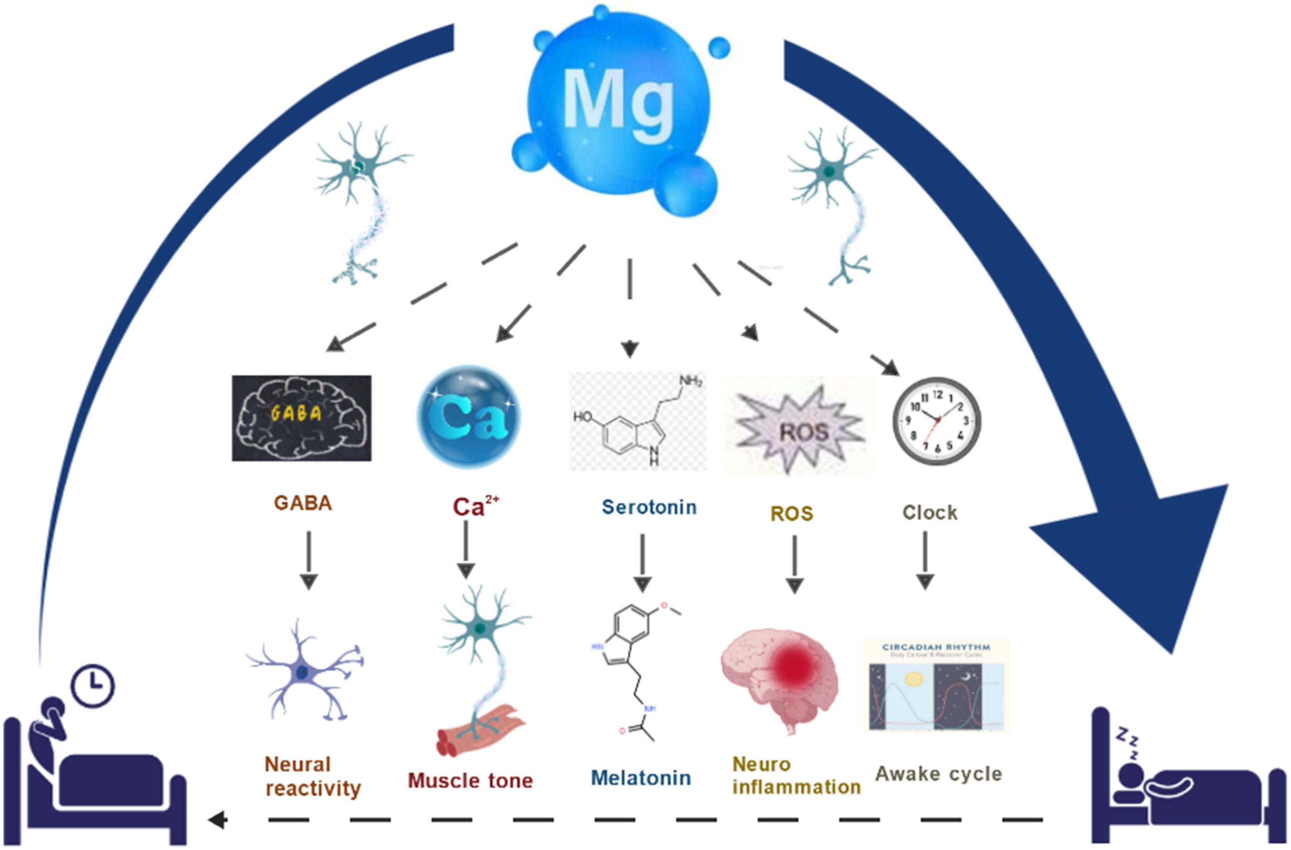

Figure 2 The mechanisms of magnesium in sleep disorder. Created with BioGDP.com.[26]
Abbreviations: GABA, gamma-aminobutyric acid; ROS, reactive oxygen species.

occurring amino acid derivative in animal organisms, functions as a homologue of L-glutamate and serves as a key excitatory neurotransmitter receptor agonist in the central nervous system. The NMDA receptor, situated within the suprachiasmatic nucleus, is a subtype of ionotropic glutamate receptors. The voltage-dependent blocking action of Mg^{2+} on NMDA-gated ion channels has been thoroughly elucidated. Magnesium, by inhibiting the NMDA receptor,[28,29] suppresses the calcium ion concentration within muscle cells, which promotes muscle relaxation and subsequently facilitates sleep.[30–32] Meanwhile, it further dilates blood vessels throughout the body and lowers the body temperature, thereby enhancing the quality of sleep.[33]

Beyond its involvement in the glutamatergic system, magnesium exerts a pivotal influence on sleep through the regulation of the GABAergic system. GABA, also known as aminobutyric acid, is a bioactive non-proteinogenic amino acid celebrated for its inhibitory characteristics. Mg^{2+} ions interact with GABA receptors,[28] potentiating GABAergic neurotransmission and subsequently dampening neural excitability, thereby facilitating the onset and maintenance of sleep.[34,35] Experimental evidence from magnesium-deficient rat models bolsters this mechanism. Monitoring electroencephalogram (EEG) activity during auditory stimulation in these animals revealed significant modifications in spike potential patterns. These electrophysiological alterations correlated with observable behavioral changes, strongly suggesting that magnesium deficiency heightens central nervous system excitability. Such findings provide robust electrophysiological validation for the link between magnesium status and neural hyperexcitability.[36] The intricate relationship between glutamate and GABA further underscores magnesium's regulatory role in sleep homeostasis. As the metabolic precursor of GABA, glutamate must be maintained in delicate equilibrium with its inhibitory counterpart to ensure proper sleep regulation. Acting as both an NMDA receptor antagonist and a GABA receptor agonist, magnesium exerts a dual-pronged modulation of neural excitability. This dual action enables magnesium to fine-tune sleep processes, exerting a particularly profound impact on the quality and architecture of slow-wave sleep (SWS), a critical phase for physiological restoration and cognitive consolidation.[31,37]

Magnesium in the Conduction of Ca^{2+} and K^+ Ion Channels

As a calcium antagonist, magnesium assumes a critical role in sleep regulation. Mg^{2+} is capable of inhibiting the Ca^{2+}-PKC second messenger system, thereby influencing associated neurotransmission processes. Additionally, it stimulates the Na^+-K^+-ATPase enzyme, contributing to the overall modulation of sleep mechanisms.[38] Magnesium contributes to sleep improvement by influencing ion channel conductance, including the conductivity of the NMDA receptor pore mentioned above[39] and the unilateral entry of potassium channels. Research has demonstrated that magnesium fulfills a vital role in hundreds of metabolic reactions and muscle functions. The NMDA receptor constitutes a unique dual-gated channel, regulated by both neurotransmitter gating and voltage gating. Under typical neuronal membrane potentials, Mg^{2+} ions occupy the NMDA receptor pore.[28] When neurons depolarize, Mg^{2+} ions dissociate, allowing Ca^{2+} and Na^+ ions to pass through the receptor pore.[29] Magnesium deficiency results in heightened neuronal excitability and augmented neuromuscular transmission.[40] Magnesium is capable of blocking calcium, a mechanism that facilitates the regulation of nerves and muscles, thereby rendering muscles more susceptible to relaxation.[41] In cases of magnesium deficiency, calcium remains unblocked, inducing excessive neural activity and triggering muscle contractions, which in turn disrupt sleep.[42]

Furthermore, given that the homeostasis of calcium and magnesium depends on shared regulatory hormones and ion transporters for their absorption, the bioavailability of magnesium may be contingent upon calcium concentration or the calcium-to-magnesium ratio (Ca: Mg).[43] Mg^{2+} is intricately linked to Ca^{2+} homeostasis, and Ca^{2+} is responsible for regulating a diverse array of physiological functions, including sleep. It has been established that fluctuations in calcium levels and intracellular potentials govern cortical slow-wave oscillations—hallmark features of SWS.[44] More recently, associations between Ca^{2+} levels, sleep latency, and non-restorative sleep have also been documented.[45] Results from a longitudinal study revealed an association between the calcium-to-magnesium ratio (highest vs lowest quartiles) and sleep duration exceeding 9 hours. However, the relatively small number of participants with a sleep duration exceeding 9 hours may have led to confidence intervals with a large margin of error, underscoring the need for future studies with larger sample sizes.[12] In a study involving 100 airline pilots, it was found that those with poor sleep quality exhibited significantly lower levels of both magnesium and calcium (both $P<0.001$). Logistic regression analysis identified Mg^{2+}

and Ca^{2+} as biomarkers associated with poor sleep quality among airline pilots (both $P<0.001$), suggesting that the concentrations of serum Mg^{2+} and Ca^{2+} may be related to poor sleep in airline pilots.[46]

Magnesium in Inflammation and Oxidative Stress

In preclinical, epidemiological, and clinical human studies, magnesium deficiency, low serum magnesium levels, and reduced dietary magnesium intake have consistently been linked to heightened production of reactive oxygen species (ROS), low-grade inflammation, and elevated levels of inflammatory markers and pro-inflammatory molecules—including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), vascular cell adhesion molecule-1 (VCAM-1), plasminogen activator inhibitor-1 (PAI-1), complement proteins, α2-macroglobulin, and fibrinogen.[47–50] Recent research has further identified a significant negative correlation between serum magnesium levels and serum malondialdehyde (MDA)—a marker of oxidative stress.[51] Magnesium deficiency induces augmented production of ROS, leading to increased generation of hydrogen peroxide and heightened production of superoxide anions by inflammatory cells. This not only exacerbates oxidative stress but also impairs antioxidant defense capacity.[48,52] Additionally, a study has found that magnesium deficiency causes excessive ROS production and low-grade inflammation, which in turn accelerates the depletion of telomeres and affects sleep.[53] Meanwhile, Magnesium is indispensable for the normal functioning of γ-glutamyl transpeptidase, an enzyme that fulfills a critical role in the synthesis of the antioxidant glutathione.[54] It has also been confirmed that magnesium possesses a mild antioxidant effect.[55]

Current research has further confirmed that low dietary magnesium intake is associated with elevated plasma C-reactive protein (CRP) levels.[50,56] CRP serves as a marker of inflammatory stress, and one possible factor contributing to increased inflammatory stress is sleep disruption or sleep deprivation.[57] Inadequate sleep duration has been linked to elevated levels of various inflammatory biomarkers, including plasma CRP. Similarly, sleep quality is associated with increased morning concentrations of the inflammatory biomarker interleukin-6 in healthy adults, elderly women, and spouses caring for individuals with Alzheimer's disease.[57] Consequently, subclinical magnesium deficiency may contribute to sleep disruption or sleep deprivation by exacerbating inflammation or oxidative stress. Conversely, chronic inflammatory stress can be mitigated by increasing magnesium intake, a measure that may enhance sleep quality and elevate red blood cell magnesium levels. Some studies have found that, compared with sodium citrate placebo, magnesium citrate supplementation reduced the plasma CRP levels of participants. This indicates that subclinical magnesium deficiency may exacerbate conditions contributing to chronic inflammatory stress. However, the findings also indicated that sleep quality improved across all participants, a phenomenon that may be attributed to the placebo effect.[9]

Magnesium in Melatonin and Serotonin

A multitude of biological hormones and neurotransmitters are involved in the sleep-wake cycle, including serotonin (5-HT), orexin, melatonin, galanin, norepinephrine, and histamine, to name a few. These brain-targeting neurotransmitters exert a substantial influence on both sleep quality and duration.[58]

Several studies have demonstrated that magnesium deficiency in rats results in a reduction in plasma melatonin concentrations.[10,59] Magnesium is closely related to the production of melatonin. As a well-investigated and widely utilized sleep-promoting hormone, melatonin is a key regulator of the sleep-wake cycle and exhibits potent antioxidant properties.[60] An increase in oxidative stress may account for, at least in part, the poor sleep quality.[61] Melatonin can enhance the activity of superoxide dismutase, thereby preventing oxidative stress-induced damage to cell membranes.[62] When combined with omega-3 fatty acids, melatonin exerts an antioxidant effect by significantly enhancing superoxide dismutase activity in the human body.[63] Furthermore, endogenous melatonin has been shown to attenuate the excitatory neurotransmitter effects of L-glutamate by inhibiting specific NMDA receptor binding sites,[64,65] thus promoting sleep.

Magnesium can also enhance the activity of serotonin N-acetyltransferase—an enzyme critical for melatonin synthesis.[59] Physiologically, magnesium interacts with the synthesis of serotonin and melatonin. Serotonin is an intermediate product in the production of melatonin, and melatonin is a metabolite of serotonin. The production of melatonin requires serotonin, and a deficiency or excess of serotonin can exert an impact on sleep duration and quality. Serotonin was first discovered in the serum, also known as 5-hydroxytryptamine. It is widely present in mammalian

https://doi.org/10.2147/NSS.S552646

tissues, especially in high concentrations in the cerebral cortex and nerve synapses. It is also an inhibitory neurotransmitter. The part of the brain responsible for regulating sleep also has serotonin receptors. Magnesium also helps monoamine substances (such as serotonin) bind to their respective sites.[39] The commonly discussed mechanism for increasing sleep duration is the pathway that promotes serotonin synthesis. Serotonin regulates most brain functions—including the sleep cycle—either directly or indirectly. Typically, serotonergic neurons collectively innervate numerous brain regions involved in sleep-wake behavior, functioning to promote consciousness and inhibit sleep.[66–68] 5-hydroxytryptophan is generated from tryptophan through the catalysis of tryptophan hydroxylase and then converted into serotonin by the catalysis of 5-hydroxytryptophan decarboxylase. Tryptophan[69] is a precursor to the neurotransmitter serotonin and the neurosecretory hormone melatonin, both of which are associated with sleep and alertness.[24,25] Tryptophan can also regulate sleep and the circadian rhythm by increasing melatonin levels.[70]

In addition, several studies have demonstrated that magnesium exerts a relaxant effect. Magnesium supplementation can reduce the concentration of serum cortisol (a stress hormone[10,31]) and thus calm the central nervous system,[71] potentially improving sleep quality. The mechanism may involve magnesium's direct effect on the function of P-glycoprotein—a blood-brain barrier transporter that, in turn, influences the entry of corticosteroid hormones into the brain.[72]

Magnesium in the Biological Clock and Circadian Rhythm

The biological clock is fundamental to the biology of most eukaryotic organisms. Through a complex network of clock-controlled genes, it coordinates behavioral and physiological processes to align with the environmental day-night cycles.[73,74] A recent study has indicated that magnesium can regulate the cellular biological clock, energy balance, and circadian rhythm, and it appears to exert a pivotal role in sleep regulation.[75] A study by Feeney et al reported the circadian rhythm of the intracellular magnesium ion concentration.[75] In human cells, algal plants, and fungi, it was found that in each organism, the level of magnesium ions in the cells, $[Mg^{2+}]i$, rises and falls within the daily cycle rhythm. Such fluctuations play a vital role in maintaining the 24-hour rhythm of the cells.[75]

Given the critical role of Mg^{2+} as an ATP cofactor, one functional outcome of intracellular Mg^{2+} ($[Mg^{2+}]i$) fluctuations is the dynamic regulation of cellular energy expenditure across the daily cycle. That is, it has a significant impact on the cell's metabolism throughout the day and how quickly the cell can convert nutrients into energy. The bioavailability of intracellular Mg^{2+} enables the global regulation of triphosphate nucleotide turnover, a process with the potential to impact over 600 MgATP-dependent enzymes in the cell, as well as all cellular systems where MgNTP hydrolysis acts as the rate-limiting step.[76] It was also discovered that the circadian control of translation by the mammalian target of rapamycin is regulated by the $[Mg^{2+}]i$ fluctuations.[77]

Magnesium in Sleep Structure and EEG

Sleep quality is an aggregate measure of sleep parameters, including sleep duration and the presence of sleep disturbances. It can be objectively assessed using polysomnography and actigraphy, and subjectively evaluated through instruments such as sleep diaries and self-reports.[35] Subjective sleep quality refers to the retrospective evaluation of sleep experiences. The most commonly used and effective assessment tool is the Pittsburgh Sleep Quality Index (PSQI), which comprises seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction over the past month.[78]

The link between magnesium and sleep quality is substantiated by prior animal and human studies.[31,39,79] According to the data from the National Health and Nutrition Examination Survey (NHANES),[80] there exists a U-shaped relationship between dietary magnesium intake and sleep duration. This could indicate the potential benefits of increasing dietary magnesium intake for poor sleep quality, encompassing both short-term and long-term sleep patterns. A clinical trial demonstrated that 8 weeks of consecutive magnesium supplementation significantly increased sleep duration and reduced sleep latency in elderly individuals.[10] In addition, magnesium treatment for patients with alcohol dependence (who often have magnesium metabolic disorders) using the PSQI significantly reduced the sleep onset latency, which decreased from an average of 40.6 min before treatment to 21.7 min (P=0.03), and improved the subjective sleep quality.[81] Interestingly, a study identified a negative correlation between magnesium intake and daytime sleepiness in women, but not in men.

Compared with the placebo group, the experimental group (receiving 500 mg of daily magnesium supplementation) showed improvements in sleep efficiency, sleep duration, sleep onset latency, and early-morning awakening frequency.[82] A study performed on rats revealed a strong correlation between forebrain magnesium concentration and sleep duration.[39] A recent systematic review, encompassing 7582 participants from 9 published cross-sectional, cohort, and randomized controlled studies, also identified an association between magnesium status and sleep quality.[83] The findings demonstrated that in healthy adults, higher magnesium intake was correlated with various sleep quality parameters, including daytime sleepiness, drowsiness, snoring, and sleep duration. Moreover, randomized controlled trials recorded positive impacts of magnesium supplementation on PSQI scores, sleep efficiency, and sleep duration.[83]

During the sleep process, various changes occur in the EEG, and these changes vary depending on the depth of sleep. Sleep can be categorized into two states—NREM sleep (also referred to as SWS) and REM sleep—based on the presence or absence of paroxysmal REM and distinct EEG wave characteristics. The sleep EEG serves as an indicator reflecting central nervous system function.[84] In the elderly population, several distinct sleep-related changes can be detected via EEG: diminished sleep continuity, shortened REM sleep latency, reduced SWS, and increased nighttime awakenings.[85,86] A study found that 27 patients in a parasomnia state with magnesium deficiency had abnormal nighttime EEGs during SWS.[87] A study involving 12 elderly participants (aged 60–80 years) by oral Mg^{2+} supplementation demonstrated that Mg^{2+} partially reversed age-related changes in the sleep EEG: it increased SWS from 10.1 min to 16.5 min ($P<0.05$) and elevated δ power and σ power during NREM sleep.[31] In animal studies, Mg^{2+} deficiency has also been shown to induce sleep disorders in rats, characterized by increased awakenings—either at the cost of reduced SWS[88] or dominated by active awakenings accompanied by a decrease in total sleep time.[89] In addition, after intravenous administration of Mg^{2+} to healthy young subjects, consistent research results such as an increase in the brain electrical power within the σ frequency range of NREM sleep were also found.[90]

Held et al further postulated that the role of Mg^{2+} in sleep architecture, particularly in SWS, is likely intricately linked to the activities of both the glutamatergic and GABAergic systems.[31] Experimental evidence supports this hypothesis: upon intracerebral injection of the NMDA receptor antagonist DL-2-amino-5-phosphonovaleric acid (APV)[91] into the thalamus and intraperitoneal injection of another NMDA receptor antagonist, MK-801,[92] a notable increase in SWS was observed in rats. Moreover, the GABAA receptor agonist THIP (gaboxadol) has been shown to augment the δ activity during SWS in both humans[93] and rats.[94,95] These findings collectively indicate that the influence of Mg^{2+} on the sleep EEG may stem from its dual role as an NMDA antagonist and a GABA agonist. Mg^{2+} may regulate the balance between excitatory and inhibitory neural signals in the central nervous system, thereby affecting the quality and duration of SWS.[90]

Magnesium in Sleep Disorders

Magnesium in Insomnia

Insomnia stands as the most prevalent sleep disorder.[96] According to the International Classification of Sleep Disorders, the diagnosis of insomnia includes difficulties in initiating sleep, maintaining sleep, and subsequent impairment of daytime functioning.[23] Characteristically, it is marked by dissatisfaction with sleep duration or quality, challenges in falling asleep or staying asleep, along with notable discomfort and disruption to daily activities.[97] Currently, validated sleep questionnaires such as the Insomnia Severity Index (ISI)[10] and the PSQI[9] are commonly employed for the diagnosis of insomnia and tracking treatment outcomes. Additionally, EEG during sleep (sleep EEG)[31] or detailed sleep diaries recorded by subjects are frequently utilized to measure and assess insomnia.

In a human study, it was observed that long-term sleep deprivation decreased intracellular magnesium content and reduced exercise tolerance, which could subsequently be corrected through oral magnesium supplementation.[98] Nielsen et al conducted a study investigating the role of magnesium supplementation in adult sleep disorders, and following 7 weeks of treatment with 320 mg/day of magnesium citrate, patients exhibited an overall improvement in their PSQI scores.[9,99] Abbasi et al aimed to examine the effects of magnesium on insomnia in elderly individuals,[10] and he administered 500 mg/day of magnesium to 46 elderly participants experiencing primary insomnia over an 8-week period, with outcomes including increased sleep duration and efficiency, as well as reduced ISI scores and sleep onset latency. Additionally, it improved objective indicators of insomnia, such as the concentrations of serum renin, melatonin, and serum cortisol.[10] Three randomized controlled trials involving 151 elderly participants across three countries compared the effects of oral magnesium with placebo. A systematic review and meta-analysis highlighted that, compared to placebo, magnesium supplementation reduced sleep onset latency by 17.36 min (P=0.0006) and extended total sleep time by 16.06 min, supporting the use of oral magnesium supplements (up to three times a day, with each dose less than 1 g) for treating insomnia symptoms.[31] Rondanelli et al found that, compared to placebo capsules, administering a formulation containing melatonin, magnesium, and zinc to 43 elderly subjects with primary insomnia, one hour before bedtime over an 8-week period, enhanced sleep quality and increased the total sleep time as measured by wearable arm sensors.[100] More recently, preliminary research by Honiak et al also concluded that magnesium supplementation could serve as a valuable alternative therapy for patients with insomnia.[11]

Another study found that a novel nutritional blend consisting of tryptophan, glycine, magnesium, tart cherry powder, and L-theanine shortened sleep onset latency (P=0.002), increased total sleep time (P=0.01), improved sleep efficiency (P=0.03), and reduced morning drowsiness (P=0.02).[101] On the other hand, in a double-blind trial involving surgical patients, the sleep-stabilizing effect of Mg^{2+} was reported. Intravenous administration of Mg^{2+} before surgery significantly improved patients' sleep quality.[102] Depoortere et al demonstrated that magnesium deficiency in rats could disrupt the normal sleep-wake cycle by increasing wakefulness and reducing SWS, and this effect was reversed upon the reintroduction of magnesium into their diet.[88]

In the treatment of insomnia, as an adjuvant therapy, magnesium not only acts as a natural NMDA antagonist and GABA agonist but also has a relaxing effect. Magnesium deficiency can cause muscle cramps, leading to poor sleep. Moreover, magnesium can increase melatonin levels, aiding in the maintenance of a normal biological clock and the alleviation of insomnia symptoms.[10,103] Another study further indicated that magnesium may alleviate insomnia associated with restless legs syndrome. Additionally, the serotonergic system represents another pathway potentially modulated by magnesium.[42]

Magnesium in Idiopathic Hypersomnia and Narcolepsy

Idiopathic hypersomnia and narcolepsy are rare chronic sleep disorders that can impair patients' cognitive function, social functioning, and health-related quality of life.[13] Their primary characteristic is excessive daytime sleepiness, with many narcolepsy patients also experiencing cataplexy. In addition, narcolepsy is associated with nighttime sleep disturbances, hypnagogic and hypnopompic hallucinations, as well as sleep paralysis. For idiopathic hypersomnia, extended nighttime sleep and sleep inertia are commonly observed.[104,105] Tunc et al conducted a study on 938 elderly outpatient patients and found that hypomagnesemia in the elderly is associated with excessive daytime sleepiness.[11] Recent research has also revealed a positive correlation between the Magnesium Deficiency Score and excessive sleep, especially among non-depressed elderly individuals.[12]

An increase in SWS during compensatory stages 1 and 2, along with a shortening of REM sleep, contributes to increased excessive sleepiness in the elderly.[106] Moreover, elderly individuals experiencing excessive sleepiness often exhibit impaired healthy eating habits, which may elevate the risk of malnutrition and consequently reduce magnesium intake.[106] Thus, a bidirectional relationship may exist between magnesium deficiency and excessive sleepiness. Nevertheless, further research is required to validate this hypothesis.

In the United States, an oral solution of sodium oxybate (Xywav), which contains unique cations such as calcium, magnesium, and potassium alongside sodium oxybate, has been approved for treating cataplexy or excessive daytime sleepiness in adults and children aged 7 years and older diagnosed with narcolepsy. It is also the first medication approved for the treatment of idiopathic hypersomnia in adults.[107,108] The efficacy and safety of sodium oxybate in the treatment of narcolepsy have been widely evaluated.[109] The European guidelines for narcolepsy strongly recommend sodium oxybate for the treatment of cataplexy and EDS in both children and adults with narcolepsy.[110] Sodium oxybate is a central nervous system depressant and an endogenous compound associated with the neurotransmitter GABA. Although the mechanism of action underlying low-dose sodium oxybate in the treatment of narcolepsy and idiopathic hypersomnia remains incompletely elucidated, it is postulated to involve the influence of GABAB receptors on noradrenergic, dopaminergic, and thalamocortical neurons during sleep.[107]

Magnesium in OSA

Obstructive sleep apnea (OSA) is defined by recurrent partial or complete collapse of the upper airway during sleep. Disruptions in respiratory airflow occur when the tongue and surrounding soft tissue structures prolapse into the pharynx due to gravitational forces and muscle relaxation, leading to a physical obstruction of the airway. These episodes lead to a complete or partial reduction in airflow and recurrent arousals.[111,112]

Karamanli et al reported that the average serum Mg level in patients with mild OSA was significantly higher than that in the severe OSA group (P=0.003), and multivariate regression analysis indicated a significant correlation between serum Mg levels and AHI (P=0.01).[14] In an observational study by Jiao et al, the blood Mg levels of OSA patients (n=39) increased significantly after Roux-en-Y gastric bypass (RYGB) surgery compared with pre-intervention levels.[15] In a cross-sectional study by Xu et al, twenty-two of the 33 patients with OSA were followed up after three months of continuous positive airway pressure treatment.[113] Observations indicated a rise in serum Mg levels. Additionally, the Pearson correlation coefficient between serum Mg and the AHI approached statistical significance (P=0.056). The multivariate logistic regression analysis revealed that individuals with serum Mg levels at or above 1.98 mg/dL were identified as having a protective factor against the severity of OSA. Specifically, when compared to those with serum Mg levels below 1.98 mg/dL, this group exhibited a significantly lower likelihood of developing severe OSA (P= 0.006).[113] These research findings demonstrate that individuals with OSA exhibit significantly lower serum Mg levels compared to healthy control subjects. The intensity of OSA seems to exert a detrimental effect on serum Mg concentrations, with these levels typically showing a marked improvement following therapeutic intervention, in parallel with the amelioration of OSA severity. The analysis by Zahraa et al also suggests that the severity of OSA affects serum Mg levels; the higher the AHI, the lower the serum Mg.[114] A recent study has also found a significant positive correlation between the Magnesium Deficiency Score and sleep apnea.[12]

However, it remains unclear whether a decrease in serum Mg levels is one of the risk factors for OSA, or whether OSA directly leads to a decrease in serum Mg levels. Furthermore, the precise direct mechanism through which a reduction in serum Mg levels might contributes to the development of OSA remains elusive. Low Mg levels might contribute to the development of OSA. According to the study by Orru et al Intermittent nocturnal hypoxia exhibits a significant association with oxidative stress, an elevation in pro-inflammatory markers, as well as OSA.[115] Similarly, in a placebo-controlled study by Nelson et al revealed that rectifying a state of low magnesium through supplementation led to an amelioration of markers associated with inflammation and oxidative stress in adults suffering from poor sleep quality.[9] Since Mg functions as a cofactor for over 325 enzymes within the human body, diseases related to the availability or function of Mg are believed to promote oxidative stress.[116] A study[12] has speculated that inflammation and oxidative stress induced by magnesium deficiency have the potential to inflict damage upon respiratory tract tissues, thereby heightening the susceptibility to airway collapse and potentially contributing to an increased incidence of sleep apnea. Moreover, magnesium plays an integral role in hundreds of enzymatic reactions within biological systems, affecting important physiological activities such as nerve conduction and muscle contraction. Magnesium deficiency may impact the normal function of the respiratory muscles by affecting the conduction function of the nervous system, or it may directly act on muscle relaxation, leading to respiratory muscle dysfunction, especially in the respiratory muscles surrounding the pharynx, thereby elevating the incidence rate of sleep apnea. On the other hand, protracted sleep apnea has the potential to induce chronic hypoxia within the human body, which in turn interferes with the metabolism and absorption of magnesium, resulting in a decrease in magnesium levels within the body. The relationship among OSA, oxidative stress, and Mg levels forms an intertwined causal chain that warrants further investigation.

Magnesium in RLS/WED

Restless legs syndrome/Willis-Ekbom disease (RLS/WED) is a sensorimotor disorder characterized by abnormal sensations in the legs. Patients frequently experience a pronounced urge to move the affected limbs. These abnormal sensations are either partially or entirely expressed in the form of voluntary movements, such as walking.[117] These symptoms typically exhibit exacerbation during sleep and commonly precipitate sleep disturbances. This disease is categorized into two types: idiopathic and secondary. Pregnancy, uremia, iron deficiency, diabetes, and neuropathy are recognized as risk factors for the secondary variant of the disease.[8] Nevertheless, the underlying pathophysiological mechanism of this disease remains incompletely.[118]

A study has shown that patients with RLS/WED have lower magnesium levels compared to healthy control groups.[119] Several research investigations have similarly indicated that both oral and intravenous magnesium supplementation can be advantageous for these patients.[9,16] Sinniah et al reported that a patient with RLS/WED made a full recovery after receiving an intravenous injection of magnesium sulfate.[17,120] Additionally, another study suggests that oral magnesium supplementation may alleviate symptoms in individuals with moderate RLS.[121] For patients with mild to moderate RLS or insomnia associated with periodic limb movements during sleep, magnesium could serve as a viable alternative therapeutic option.[121] In the study of pregnant women, Yıldırım found that the concentrations of zinc and magnesium in pregnant women afflicted with this disease were significantly lower compared to those observed in other women. Furthermore, the study also established a correlation between these levels and the severity of the syndrome symptoms. Specifically, there was an inverse relationship such that patients with lower serum magnesium and zinc levels presented with more severe symptoms.[16] This suggests that magnesium may be regarded as a suitable alternative treatment for patients with RLS/WED. More recently, the study by Honiak et al also reached the same conclusion, indicating that magnesium supplementation has the potential to serve as a beneficial alternative therapeutic approach for patients diagnosed with RLS.[11]

Magnesium may potentially participate in the pathophysiology of RLS/WED. A number of studies have demonstrated that magnesium assumes a pivotal role in hundreds of metabolic reactions and is crucial for proper muscle function.[122,123] Magnesium deficiency has the potential to induce neuronal excitability and augment neuromuscular transmission.[40] This may be attributed to magnesium's ability to block calcium, a mechanism that aids in regulating nerves and muscles, thereby facilitating muscle relaxation.[41] When magnesium levels are low, calcium is not adequately blocked, leading to neural overactivity. This overactivity triggers muscle contractions, which in turn result in abnormal sensations in the leg muscles. The serotonergic system represents another potential pathway that may be modulated by magnesium.[42]

Conversely, in a prospective case—control study encompassing 600 pregnant women diagnosed with RLS/WED, the investigators discovered that a reduction in iron intake and an elevation in magnesium consumption were correlated with an exacerbation of the syndrome's symptoms.[124] In a systematic review, Nathaniel et al posited that reliable conclusions regarding the efficacy of magnesium in the treatment of RLS/WED cannot be drawn. They asserted that, at present, it remains uncertain whether magnesium can alleviate the symptoms of RLS/WED.[9] In a thorough and all-encompassing assessment of both pharmacological and non-pharmacological treatment modalities for RLS/WED, Anguelova et al expressed the view that magnesium does not constitute a valuable therapeutic agent for alleviating the symptoms of this disease.[18]

The pathophysiology of the disease in pregnant women may diverge from that in non-pregnant women, which serves as one of the contributing factors to the aforementioned difference. In Nathaniel's study, only 22 men and 78 women were included.[9] The sample size was insufficient and biased towards women. Estrogen may have a potential impact on melatonin,[125] thereby affecting sleep. For patients with multiple sleep disorders, magnesium therapeutic agents may have a positive effect on the main type of sleep disorders, but their improvement effect on the secondary types of sleep disorders is not obvious or is masked. In addition, placebos can also affect the subjective results of sleep tests. More research is still needed in the future to rule out biases related to age, gender and disease type. Higher-quality, comprehensive, and systematic studies may be needed to clarify the pharmacological effect of magnesium on RLS/WED.

Limitations and Future Directions

While current research has established a strong link between magnesium and sleep disorders, the specific mechanisms underlying magnesium's role in sleep regulation still contain numerous unanswered questions. Firstly, the fragmented nature of mechanistic explanations is striking: existing studies tend to concentrate on isolated pathways (eg, activation of the GABAergic system, modulation of melatonin synthesis, or suppression of oxidative stress), yet the overarching mechanism through which magnesium influences sleep architecture via cross-system crosstalk—such as the synergistic interplay of neurotransmitter balance, circadian rhythm control, and inflammatory responses—has yet to be clarified. Secondly, research design is marked by notable limitations: most investigations depend on clinical regression analyses, which are susceptible to bias. Furthermore, these studies merely show a strong correlation between magnesium and sleep disorders without establishing a definitive causal relationship or determining whether bidirectional causality exists between the two. Additionally, the role of population heterogeneity remains poorly understood: patients with distinct types of sleep disorders (including insomnia and sleep apnea syndrome) exhibit differential responses to magnesium-based interventions. Moreover, there is insufficient stratified analysis data regarding how factors like age, gender, and genetic background influence magnesium's sleep-regulating effects.

Moving forward, efforts should be made to develop a molecular network landscape of magnesium-mediated sleep regulation using multi-omics approaches (eg, transcriptomics and metabolomics), aiming to elucidate the interactive mechanisms across neurotransmitter, endocrine, and immune pathways. Secondly, more high-quality clinical translational research is needed, integrating wearable devices for real-time monitoring of sleep parameters and magnesium ion levels, to define the magnesium intervention thresholds and optimal supplementation protocols for different sleep disorder subtypes. In sleep studies, magnesium oxide, magnesium citrate or magnesium L-aspartate were used as interventions. And magnesium glycinate and magnesium threonate are widely used and not very expensive in clinical practice. In the future, more drugs combining magnesium with other trace elements or vitamins can be developed (Figure 3).

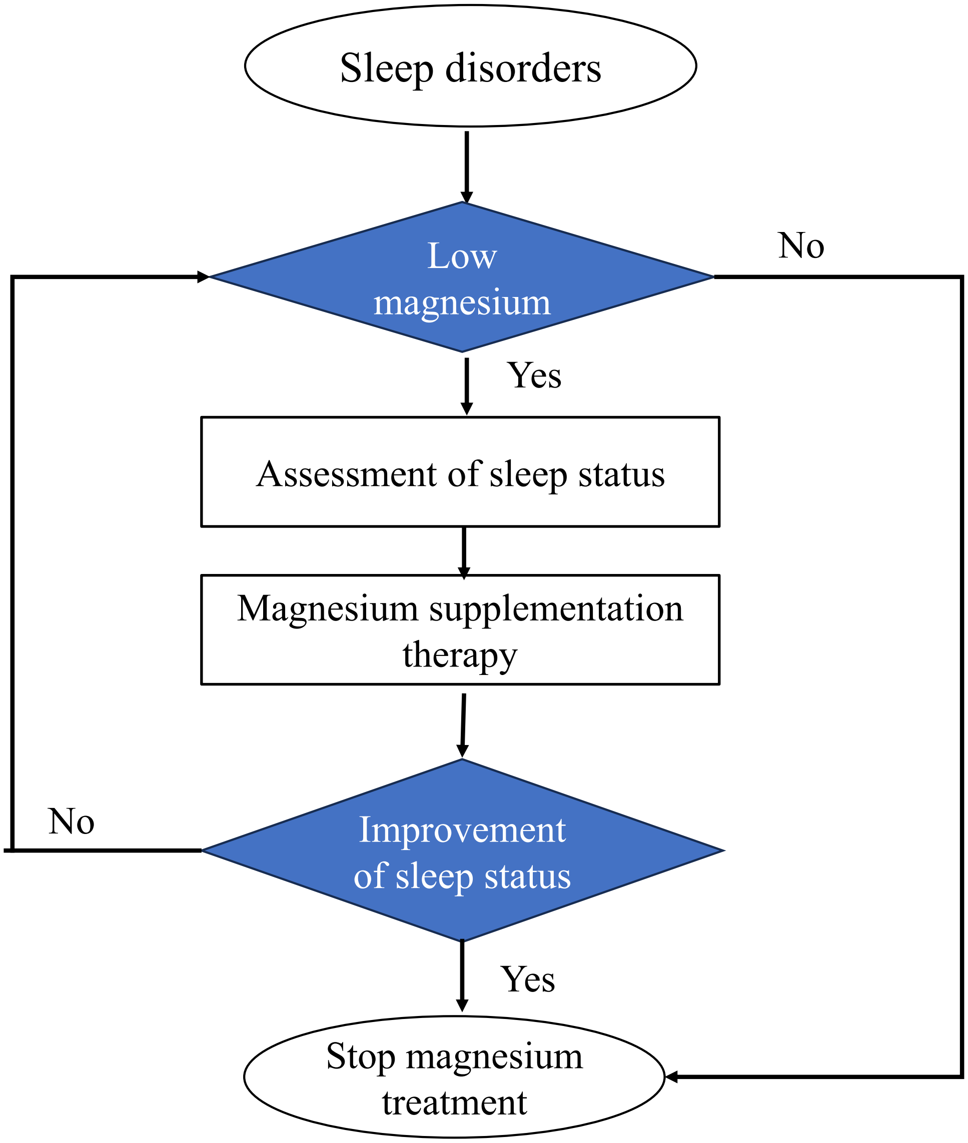

Figure 3 A decision-making flowchart of magnesium therapy in sleep disorders.

Conclusion

As sleep disorders have emerged as a prevalent concern in daily life, research on sleep and sleep-related diseases has perhaps become more crucial than ever before. In recent years, the role of magnesium in sleep disorders has garnered substantial attention. Further exploration of magnesium's function in sleep health may help elucidate the physiological mechanisms underlying sleep health and the pathophysiology of sleep disorders. Magnesium is involved in sleep disorders through various mechanisms. An increasing body of evidence suggests a bidirectional relationship between magnesium deficiency and sleep disorders. In specific sleep disorders, magnesium deficiency can contribute via two or more mechanisms, which may exhibit a synergistic effect. Magnesium deficiency may elevate neural excitability, increase muscle tension or exacerbate oxidative stress responses, thereby impairing the synthesis of sleep-inducing hormones, altering normal circadian rhythms and sleep architecture. Conversely, sleep disorders can disrupt dietary magnesium intake and its absorption in the gastrointestinal tract, thereby contributing to magnesium deficiency in the body. However, high-quality, comprehensive, and systematic investigations are still required to clarify the mechanisms underlying the association between magnesium and sleep disorders, laying a solid foundation for the clinical application of bidirectional interventions. Magnesium supplementation can be integrated with traditional pharmacological and non-pharmacological interventions to implement comprehensive management strategies, offering new entry points for the diagnosis and treatment of these diseases.

Highlights

1. Magnesium regulates sleep health through multiple physiological mechanisms.
2. Magnesium intervention has improving effects on certain sleep disorder diseases.
3. There is a bidirectional association between magnesium deficiency and sleep disorders.

Abbreviations

GABA, gamma-aminobutyric acid; NREM, non-rapid eye movement; REM, rapid eye movement; NMDA, N-methyl-D-aspartic acid; EEG, electroencephalogram; CRP, C-reactive protein; PSQI, Pittsburgh Sleep Quality Index; SWS, slow-wave sleep; ISI, Insomnia Severity Index; OSA, Obstructive sleep apnea; RLS, Restless legs syndrome; WED, Willis-Ekbom disease.

Data Sharing Statement

Data sharing is not applicable to this article as no data were created or analysed in this paper.

Author Contributions

Conceptualization: M.Y. and C.J.H.; methodology: C.J.H., J.C.X., and Y.X.Y.; investigation: C.J.H., B.W., and X.Y.C.; visualization: C.J.H.; supervision: M.Y.; writing—original draft: C.J.H., B.W., X.Y.C.; writing—review & editing: C.J. H., J.C.X., Y.X.Y. and M.Y. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the Natural Science Foundation of Hunan Province (2025JJ50615), the University of South China Clinical Research 4310 Program (20224310NHYCG08), the Clinical Medical Research Center of Hunan Province (2023SK4050), the Project of Guangxi Health Commission (Z-A20221278) and the Major Scientific Research Projects for Advanced Talents of Hunan Provincial Health Commission (R2023150).

Disclosure

No potential competing interest was reported by the author(s).

References

1. Ryan MF. The role of magnesium in clinical biochemistry: an overview. *Ann Clin Biochem*. 1991;28(Pt 1):19–26. doi:10.1177/000456329102800103
2. Saris NE, Mervaala E, Karppanen H, et al. Magnesium. An update on physiological, clinical and analytical aspects. *Clin Chim Acta*. 2000;294(1–2):1–26. doi:10.1016/S0009-8981(99)00258-2
3. Resnick LM, Barbagallo M, Dominguez LJ, et al. Relation of cellular potassium to other mineral ions in hypertension and diabetes. *Hypertension*. 2001;38(3 Pt 2):709–712. doi:10.1161/01.HYP.38.3.709
4. Hase T, Miyazaki M, Ichikawa K, et al. Short hydration with 20 mEq of magnesium supplementation for lung cancer patients receiving cisplatin-based chemotherapy: a prospective study. *Int J Clin Oncol*. 2020;25(11):1928–1935. doi:10.1007/s10147-020-01755-1
5. Lo CK, Mertz D, Loeb M. Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. *BMC Med Res Methodol*. 2014;14(1):45. doi:10.1186/1471-2288-14-45
6. Higgins JP, Altman DG, Gotzsche PC, et al. The cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343(oct18 2):d5928. doi:10.1136/bmj.d5928
7. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339(jul21 1):b2535. doi:10.1136/bmj.b2535
8. Sato-Mito N, Sasaki S, Murakami K, et al. The midpoint of sleep is associated with dietary intake and dietary behavior among young Japanese women. *Sleep Med*. 2011;12(3):289–294. doi:10.1016/j.sleep.2010.09.012
9. Nielsen FH, Johnson LK, Zeng H. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. *Magnes Res*. 2010;23(4):158–168. doi:10.1684/mrh.2010.0220
10. Abbasi B, Kimiagar M, Sadeghniiat K, et al. The effect of magnesium supplementation on primary insomnia in elderly: a double-blind placebo-controlled clinical trial. *J Res Med Sci*. 2012;17(12):1161–1169.
11. Tunc M, Soysal P, Pasin O, et al. Hypomagnesemia is associated with excessive daytime sleepiness, but not insomnia, in older adults. *Nutrients*. 2023;15(11):2467. doi:10.3390/nu15112467
12. Luo X, Tang M, Wei X, et al. Association between magnesium deficiency score and sleep quality in adults: a population-based cross-sectional study. *J Affect Disord*. 2024;358:105–112. doi:10.1016/j.jad.2024.05.002
13. Lai X, Chen W, Bian X, et al. Predictors of poor sleep quality and excessive daytime sleepiness in peritoneal dialysis patients. *Ren Fail*. 2015;37(1):61–65. doi:10.3109/0886022X.2014.959431
14. Karamanli H, Kizilirmak D, Akgedik R, et al. Serum levels of magnesium and their relationship with CRP in patients with OSA. *Sleep Breath*. 2017;21(2):549–556. doi:10.1007/s11325-016-1402-4
15. Jiao X, Zou J, Zhang P, et al. Roux-en-Y gastric bypass surgery on obstructive sleep apnea-hypopnea syndrome: factors associated with postoperative efficacy. *Obes Surg*. 2016;26(12):2924–2930. doi:10.1007/s11695-016-2209-x
16. Yildirim E, Apaydin H. Zinc and magnesium levels of pregnant women with restless leg syndrome and their relationship with anxiety: a case-control study. *Biol Trace Elem Res*. 2021;199(5):1674–1685. doi:10.1007/s12011-020-02287-5
17. Bartell S, Zallek S. Intravenous magnesium sulfate may relieve restless legs syndrome in pregnancy. *J Clin Sleep Med*. 2006;2(2):187–188. doi:10.5664/jcsm.26515
18. Anguelova GV, Vlak MHM, Kurvers AGY, et al. Pharmacologic and nonpharmacologic treatment of restless legs syndrome. *Sleep Med Clin*. 2020;15(2):277–288. doi:10.1016/j.jsmc.2020.02.013
19. Doherty R, Madigan S, Warrington G, et al. Sleep and nutrition interactions: implications for athletes. *Nutrients*. 2019;11(4):822. doi:10.3390/nu11040822
20. Hirshkowitz M, Whiton K, Albert SM, et al. National sleep foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*. 2015;1(1):40–43. doi:10.1016/j.sleh.2014.12.010
21. Ohayon M, Wickwire EM, Hirshkowitz M, et al. National sleep foundation's sleep quality recommendations: first report. *Sleep Health*. 2017;3(1):6–19. doi:10.1016/j.sleh.2016.11.006
22. Leger D, Poursain B, Neubauer D, et al. An international survey of sleeping problems in the general population. *Curr Med Res Opin*. 2008;24(1):307–317. doi:10.1185/030079907X253771
23. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest*. 2014;146(5):1387–1394. doi:10.1378/chest.14-0970
24. Espana RA, Scammell TE. Sleep neurobiology from a clinical perspective. *Sleep*. 2011;34(7):845–858. doi:10.5665/SLEEP.1112
25. Jones BE. Neurobiology of waking and sleeping. *Handb Clin Neurol*. 2011;98:131–149.
26. Jiang S, Li H, Zhang L, et al. Generic diagramming platform (GDP): a comprehensive database of high-quality biomedical graphics. *Nucleic Acids Res*. 2025;53(D1):D1670–D6. doi:10.1093/nar/gkae973
27. Alam MA, Mallick BN. Glutamic acid stimulation of the perifornical-lateral hypothalamic area promotes arousal and inhibits non-REM/REM sleep. *Neurosci Lett*. 2008;439(3):281–286. doi:10.1016/j.neulet.2008.05.042
28. Papadopol V, Nechifor M. Magnesium in neuroses and neuroticism. magnesium in the central nervous system. Adelaide (AU); 2011.
29. Na HS, Ryu JH, Do SH. The role of magnesium in pain. Magnesium in the central nervous system. Adelaide (AU); 2011.
30. Jenkinson DH. The nature of the antagonism between calcium and magnesium ions at the neuromuscular junction. *J Physiol*. 1957;138(3):434–444. doi:10.1113/jphysiol.1957.sp005860
31. Held K, Antonijevic IA, Kunzel H, et al. Oral Mg(2+) supplementation reverses age-related neuroendocrine and sleep EEG changes in humans. *Pharmacopsychiatry*. 2002;35(4):135–143. doi:10.1055/s-2002-33195
32. Bannai M, Kawai N. New therapeutic strategy for amino acid medicine: glycine improves the quality of sleep. *J Pharmacol Sci*. 2012;118(2):145–148. doi:10.1254/jphs.11R04FM
33. Barrett J, Lack L, Morris M. The sleep-evoked decrease of body temperature. *Sleep*. 1993;16(2):93–99.
34. Watanabe M, Maemura K, Kanbara K, et al. GABA and GABA receptors in the central nervous system and other organs. *Int Rev Cytol*. 2002;213:1–47. doi:10.1016/s0074-7696(02)13011-7

35. Zhang Y, Chen C, Lu L, et al. Association of magnesium intake with sleep duration and sleep quality: findings from the CARDIA study. *Sleep*. 2022;45(4). doi:10.1093/sleep/zsab276
36. Goto Y, Nakamura M, Abe S, et al. Physiological correlates of abnormal behaviors in magnesium-deficient rats. *Epilepsy Res*. 1993;15 (2):81–89. doi:10.1016/0920-1211(93)90089-P
37. Peuhkuri K, Sihvola N, Korpela R. Diet promotes sleep duration and quality. *Nutr Res*. 2012;32(5):309–319. doi:10.1016/j.nutres.2012.03.009
38. Huang FL, Huang KP. Interaction of protein kinase C isozymes with phosphatidylinositol 4,5-bisphosphate. *J Biol Chem*. 1991;266 (14):8727–8733. doi:10.1016/S0021-9258(18)31506-0
39. Chollet D, Franken P, Raffin Y, et al. Blood and brain magnesium in inbred mice and their correlation with sleep quality. *Am J Physiol Regul Integr Comp Physiol*. 2000;279(6):R2173–8. doi:10.1152/ajpregu.2000.279.6.R2173
40. Rabbitt L, Mulkerrin EC, O'Keeffe ST. A review of nocturnal leg cramps in older people. *Age Ageing*. 2016;45(6):776–782. doi:10.1093/ageing/afw139
41. Pinto MM, Dubouchaud H, Jouve C, et al. A chronic low-dose magnesium L-lactate administration has a beneficial effect on the myocardium and the skeletal muscles. *J Physiol Biochem*. 2022;78(2):501–516. doi:10.1007/s13105-021-00827-8
42. Cuciureanu MD, Vink R. Magnesium and stress. Magnesium in the Central Nervous System. Adelaide (AU); 2011.
43. Dai Q, Shu XO, Deng X, et al. Modifying effect of calcium/magnesium intake ratio and mortality: a population-based cohort study. *BMJ Open*. 2013;3(2):e002111. doi:10.1136/bmjopen-2012-002111
44. Wang Y, Minami Y, Ode KL, et al. The role of calcium and CaMKII in sleep. *Front Syst Neurosci*. 2022;16:1059421. doi:10.3389/fnsys.2022.1059421
45. Jeon YS, Yu S, Kim C, et al. Lower serum calcium levels associated with disrupted sleep and rest-activity rhythm in shift workers. *Nutrients*. 2022;14(15):3021. doi:10.3390/nu14153021
46. Minoretti P, Santiago Saez A, Garcia Martin A, et al. Serum calcium and magnesium levels, not 25-hydroxyvitamin D, are associated with sleep quality in airline pilots. *Cureus*. 2023;15(12):e50940. doi:10.7759/cureus.50940
47. King DE, Mainous AG, Geesey ME, et al. Dietary magnesium and C-reactive protein levels. *J Am Coll Nutr*. 2005;24(3):166–171. doi:10.1080/07315724.2005.10719461
48. Mazur A, Maier JA, Rock E, et al. Magnesium and the inflammatory response: potential physiopathological implications. *Arch Biochem Biophys*. 2007;458(1):48–56. doi:10.1016/j.abb.2006.03.031
49. Dominguez LJ, Veronese N, Guerrero-Romero F, et al. Magnesium in infectious diseases in older people. *Nutrients*. 2021;13(1):180. doi:10.3390/nu13010180
50. Song Y, Li TY, van Dam RM, et al. Magnesium intake and plasma concentrations of markers of systemic inflammation and endothelial dysfunction in women. *Am J Clin Nutr*. 2007;85(4):1068–1074. doi:10.1093/ajcn/85.4.1068
51. Kaliaperumal R, Venkatachalam R, Nagarajan P, et al. Association of serum magnesium with oxidative stress in the pathogenesis of diabetic cataract. *Biol Trace Elem Res*. 2021;199(8):2869–2873. doi:10.1007/s12011-020-02429-9
52. Weglicki WB, Mak IT, Kramer JH, et al. Role of free radicals and substance P in magnesium deficiency. *Cardiovasc Res*. 1996;31(5):677–682. doi:10.1016/S0008-6363(95)00196-4
53. Dhillon VS, Deo P, Thomas P, et al. Low magnesium in conjunction with high homocysteine and less sleep accelerates telomere attrition in healthy elderly Australian. *Int J Mol Sci*. 2023;24(2):982. doi:10.3390/ijms24020982
54. Tohidi M, Ghasemi A, Hadaegh F, et al. Intra-erythrocyte magnesium is associated with gamma-glutamyl transferase in obese children and adolescents. *Biol Trace Elem Res*. 2011;143(2):835–843. doi:10.1007/s12011-010-8949-x
55. Weglicki WB, Bloom S, Cassidy MM, et al. Antioxidants and the cardiomyopathy of Mg-deficiency. *Am J Cardiovasc Pathol*. 1992;4 (3):210–215.
56. Chacko SA, Song Y, Nathan L, et al. Relations of dietary magnesium intake to biomarkers of inflammation and endothelial dysfunction in an ethnically diverse cohort of postmenopausal women. *Diabetes Care*. 2010;33(2):304–310. doi:10.2337/dc09-1402
57. Simpson N, Dinges DF. Sleep and inflammation. *Nutr Rev*. 2007;65(12 Pt 2):S244–52. doi:10.1301/nr.2007.dec.S244-S252
58. Saper CB, Scammell TE, Lu J. Hypothalamic regulation of sleep and circadian rhythms. *Nature*. 2005;437(7063):1257–1263. doi:10.1038/nature04284
59. Billyard AJ, Eggett DL, Franz KB. Dietary magnesium deficiency decreases plasma melatonin in rats. *Magnes Res*. 2006;19(3):157–161.
60. Durlach J, Pages N, Bac P, et al. Biorhythms and possible central regulation of magnesium status, phototherapy, darkness therapy and chronopathological forms of magnesium depletion. *Magnes Res*. 2002;15(1–2):49–66.
61. Gopalakrishnan A, Ji LL, Cirelli C. Sleep deprivation and cellular responses to oxidative stress. *Sleep*. 2004;27(1):27–35. doi:10.1093/sleep/27.1.27
62. Morvaridzadeh M, Sadeghi E, Agah S, et al. Effect of melatonin supplementation on oxidative stress parameters: a systematic review and meta-analysis. *Pharmacol Res*. 2020;161:105210. doi:10.1016/j.phrs.2020.105210
63. Heshmati J, Morvaridzadeh M, Maroufizadeh S, et al. Omega-3 fatty acids supplementation and oxidative stress parameters: a systematic review and meta-analysis of clinical trials. *Pharmacol Res*. 2019;149:104462. doi:10.1016/j.phrs.2019.104462
64. Bavithra S, Sugantha Priya E, Selvakumar K, et al. Effect of melatonin on glutamate: bdnf signaling in the cerebral cortex of polychlorinated biphenyls (PCBs)-exposed adult male rats. *Neurochem Res*. 2015;40(9):1858–1869. doi:10.1007/s11064-015-1677-z
65. Yovanno RA, Chou TH, Brantley SJ, et al. Excitatory and inhibitory D-serine binding to the NMDA receptor. *Elife*. 2022;11. doi:10.7554/eLife.77645
66. McLean PG, Borman RA, Lee K. 5-HT in the enteric nervous system: gut function and neuropharmacology. *Trends Neurosci*. 2007;30(1):9–13. doi:10.1016/j.tins.2006.11.002
67. Oxenkrug GF. Metabolic syndrome, age-associated neuroendocrine disorders, and dysregulation of tryptophan-kynurenine metabolism. *Ann N Y Acad Sci*. 2010;1199(1):1–14. doi:10.1111/j.1749-6632.2009.05356.x
68. Szczepanska-Sadowska E, Cudnoch-Jedrzejewska A, Ufnal M, et al. Brain and cardiovascular diseases: common neurogenic background of cardiovascular, metabolic and inflammatory diseases. *J Physiol Pharmacol*. 2010;61(5):509–521.
69. Richardson GS. The human circadian system in normal and disordered sleep. *J Clin Psychiatry*. 2005;66 Suppl 9:3–9. quiz 42-3.
70. Paredes SD, Barriga C, Reiter RJ, et al. Assessment of the potential role of tryptophan as the precursor of serotonin and melatonin for the aged sleep-wake cycle and immune function: streptopelia risoria as a model. *Int J Tryptophan Res*. 2009;2:23–36. doi:10.4137/IJTR.S1129

71. Wienecke E, Nolden C. Long-term HRV analysis shows stress reduction by magnesium intake] [J. *MMW Fortschr Med*. 2016;158(Suppl 6):12–16. doi:10.1007/s15006-016-9054-7
72. Karssen AM, Meijer OC, van der Sandt IC, et al. Multidrug resistance P-glycoprotein hampers the access of cortisol but not of corticosterone to mouse and human brain. *Endocrinology*. 2001;142(6):2686–2694. doi:10.1210/endo.142.6.8213
73. Hughes ME, DiTacchio L, Hayes KR, et al. Harmonics of circadian gene transcription in mammals. *PLoS Genet*. 2009;5(4):e1000442. doi:10.1371/journal.pgen.1000442
74. Endo M, Shimizu H, Nohales MA, et al. Tissue-specific clocks in Arabidopsis show asymmetric coupling. *Nature*. 2014;515(7527):419–422. doi:10.1038/nature13919
75. Feeney KA, Hansen LL, Putker M, et al. Daily magnesium fluxes regulate cellular timekeeping and energy balance. *Nature*. 2016;532 (7599):375–379. doi:10.1038/nature17407
76. de Baaij JH, Hoenderop JG, Bindels RJ. Magnesium in man: implications for health and disease. *Physiol Rev*. 2015;95(1):1–46. doi:10.1152/physrev.00012.2014
77. Lipton JO, Yuan ED, Boyle LM, et al. The circadian protein BMAL1 regulates translation in response to S6K1-mediated phosphorylation. *Cell*. 2015;161(5):1138–1151. doi:10.1016/j.cell.2015.04.002
78. Buysse DJ, Reynolds CF, Monk TH, et al. The pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28(2):193–213. doi:10.1016/0165-1781(89)90047-4
79. Chollet D, Franken P, Raffin Y, et al. Magnesium involvement in sleep: genetic and nutritional models. *Behav Genet*. 2001;31(5):413–425. doi:10.1023/A:1012790321071
80. Grandner MA, Jackson N, Gerstner JR, et al. Dietary nutrients associated with short and long sleep duration. Data from a nationally representative sample. *Appetite*. 2013;64:71–80. doi:10.1016/j.appet.2013.01.004
81. Hornyak M, Haas P, Veit J, et al. Magnesium treatment of primary alcohol-dependent patients during subacute withdrawal: an open pilot study with polysomnography. *Alcohol Clin Exp Res*. 2004;28(11):1702–1709. doi:10.1097/01.ALC.0000145695.52747.BE
82. Cao Y, Zhen S, Taylor AW, et al. Magnesium intake and sleep disorder symptoms: findings from the jiangsu nutrition study of chinese adults at five-year follow-up. *Nutrients*. 2018;10(10):1354. doi:10.3390/nu10101354
83. Arab A, Rafie N, Amani R, et al. The role of magnesium in sleep health: a systematic review of available literature. *Biol Trace Elem Res*. 2023;201(1):121–128. doi:10.1007/s12011-022-03162-1
84. Scarpelli S, Bartolacci C, D'Atri A, et al. Electrophysiological correlates of dream recall during rem sleep: evidence from multiple awakenings and within-subjects design. *Nat Sci Sleep*. 2020;12:1043–1052. doi:10.2147/NSS.S279786
85. Bliwise DL. Sleep in normal aging and dementia. *Sleep*. 1993;16(1):40–81. doi:10.1093/sleep/16.1.40
86. Prinz PN, Peskind ER, Vitaliano PP, et al. Changes in the sleep and waking EEGs of nondemented and demented elderly subjects. *J Am Geriatr Soc*. 1982;30(2):86–93. doi:10.1111/j.1532-5415.1982.tb01279.x
87. Popoviciu L, Delast-Popoviciu D, Delast-Popoviciu R, et al. Parasomnias (non-epileptic nocturnal episodic manifestations) in patients with magnesium deficiency. *Rom J Neurol Psychiatry*. 1990;28(1):19–24.
88. Depoortere H, Francon D, Llopis J. Effects of a magnesium-deficient diet on sleep organization in rats. *Neuropsychobiology*. 1993;27 (4):237–245. doi:10.1159/000118988
89. Poenaru S, Rouhani S, Durlach J, et al. Vigilance states and cerebral monoamine metabolism in experimental magnesium deficiency. *Magnesium*. 1984;3(3):145–151.
90. Murck H, Steiger A. Mg2+ reduces ACTH secretion and enhances spindle power without changing delta power during sleep in men – possible therapeutic implications. *Psychopharmacology*. 1998;137(3):247–252. doi:10.1007/s002130050617
91. Juhasz G, Kekesi K, Emri Z, et al. Sleep-promoting action of excitatory amino acid antagonists: a different role for thalamic NMDA and non-NMDA receptors. *Neurosci Lett*. 1990;114(3):333–338. doi:10.1016/0304-3940(90)90586-X
92. Campbell IG, Feinberg I. Noncompetitive NMDA channel blockade during waking intensely stimulates NREM delta. *J Pharmacol Exp Ther*. 1996;276(2):737–742. doi:10.1016/S0022-3565(25)12350-1
93. Faulhaber J, Steiger A, Lancel M. The GABAA agonist THIP produces slow wave sleep and reduces spindling activity in NREM sleep in humans. *Psychopharmacology*. 1997;130(3):285–291. doi:10.1007/s002130050241
94. Lancel M. The GABA(A) agonist THIP increases non-REM sleep and enhances non-REM sleep-specific delta activity in the rat during the dark period. *Sleep*. 1997;20(12):1099–1104. doi:10.1093/sleep/20.12.1099
95. Lancel M, Faulhaber J. The GABAA agonist THIP (gaboxadol) increases non-REM sleep and enhances delta activity in the rat. *Neuroreport*. 1996;7(13):2241–2245. doi:10.1097/00001756-199609020-00036
96. Sharma M, Dhiman HS, Acharya UR. Automatic identification of insomnia using optimal antisymmetric biorthogonal wavelet filter bank with ECG signals. *Comput Biol Med*. 2021;131:104246. doi:10.1016/j.compbiomed.2021.104246
97. Sharma M, Darji J, Thakrar M, et al. Automated identification of sleep disorders using wavelet-based features extracted from electrooculogram and electromyogram signals. *Comput Biol Med*. 2022;143:105224. doi:10.1016/j.compbiomed.2022.105224
98. Tanabe K, Yamamoto A, Suzuki N, et al. Efficacy of oral magnesium administration on decreased exercise tolerance in a state of chronic sleep deprivation. *Jpn Circ J*. 1998;62(5):341–346. doi:10.1253/jcj.62.341
99. Cao Y, Wittert G, Taylor AW, et al. Associations between macronutrient intake and obstructive sleep apnoea as well as self-reported sleep symptoms: results from a cohort of community dwelling australian men. *Nutrients*. 2016;8(4):207. doi:10.3390/nu8040207
100. Rondanelli M, Opizzi A, Monteferrario F, et al. The effect of melatonin, magnesium, and zinc on primary insomnia in long-term care facility residents in Italy: a double-blind, placebo-controlled clinical trial. *J Am Geriatr Soc*. 2011;59(1):82–90. doi:10.1111/j.1532-5415.2010.03232.x
101. Langan-Evans C, Hearris MA, Gallagher C, et al. Nutritional modulation of sleep latency, duration, and efficiency: a randomized, repeated-measures, double-blind deception study. *Med Sci Sports Exerc*. 2023;55(2):289–300. doi:10.1249/MSS.0000000000003040
102. Tramer MR, Schneider J, Marti RA, et al. Role of magnesium sulfate in postoperative analgesia. *Anesthesiology*. 1996;84(2):340–347. doi:10.1097/00000542-199602000-00011
103. Alizadeh M, Karandish M, Asghari Jafarabadi M, et al. Metabolic and hormonal effects of melatonin and/or magnesium supplementation in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Nutr Metab*. 2021;18(1):57. doi:10.1186/s12986-021-00586-9
104. Thorpy MJ. Recently approved and upcoming treatments for narcolepsy. *CNS Drugs*. 2020;34(1):9–27. doi:10.1007/s40263-019-00689-1

105. Trotti LM, Arnulf I. Idiopathic hypersomnia and other hypersomnia syndromes. *Neurotherapeutics*. 2021;18(1):20–31. doi:10.1007/s13311-020-00919-1
106. Littner MR, Kushida C, Wise M, et al. Practice parameters for clinical use of the multiple sleep latency test and the maintenance of wakefulness test. *Sleep*. 2005;28(1):113–121. doi:10.1093/sleep/28.1.113
107. Heo YA. Calcium, magnesium, potassium and sodium oxybates (Xywav((R))) in sleep disorders: a profile of its use. *CNS Drugs*. 2022;36(5):541–549. doi:10.1007/s40263-022-00912-6
108. Dauvilliers Y, Bogan RK, Sonka K, et al. Calcium, magnesium, potassium, and sodium oxybates oral solution: a lower-sodium alternative for cataplexy or excessive daytime sleepiness associated with narcolepsy. *Nat Sci Sleep*. 2022;14:531–546. doi:10.2147/NSS.S279345
109. Robinson DM, Keating GM. Sodium oxybate: a review of its use in the management of narcolepsy. *CNS Drugs*. 2007;21(4):337–354. doi:10.2165/00023210-200721040-00007
110. Bassetti CLA, Kallweit U, Vignatelli L, et al. European guideline and expert statements on the management of narcolepsy in adults and children. *J Sleep Res*. 2021;30(6):e13387. doi:10.1111/jsr.13387
111. Osman AM, Carter SG, Carberry JC, et al. Obstructive sleep apnea: current perspectives. *Nat Sci Sleep*. 2018;10:21–34. doi:10.2147/NSS.S124657
112. Spicuzza L, Caruso D, Di Maria G. Obstructive sleep apnoea syndrome and its management. *Ther Adv Chronic Dis*. 2015;6(5):273–285. doi:10.1177/2040622315590318
113. Xu Q, Du J, Ling X, et al. Evaluation of MIh scoring system in diagnosis of obstructive sleep apnea syndrome. *Med Sci Monit*. 2017;23:4715–4722. doi:10.12659/MSM.904087
114. Al Wadee Z, Ooi SL, Pak SC. Serum magnesium levels in patients with obstructive sleep apnoea: a systematic review and meta-analysis. *Biomedicines*. 2022;10(9):2273. doi:10.3390/biomedicines10092273
115. Orru G, Storari M, Scano A, et al. Obstructive sleep apnea, oxidative stress, inflammation and endothelial dysfunction-An overview of predictive laboratory biomarkers. *Eur Rev Med Pharmacol Sci*. 2020;24(12):6939–6948. doi:10.26355/eurrev_202006_21685
116. Wyparlo-Wszelaki M, Wasik M, Machon-Grecka A, et al. Blood magnesium level and selected oxidative stress indices in lead-exposed workers. *Biol Trace Elem Res*. 2021;199(2):465–472. doi:10.1007/s12011-020-02168-x
117. Chaudhuri KR. Restless legs syndrome. *N Engl J Med*. 2003;349(8):815. doi:10.1056/NEJM200308213490819
118. Ashtiani AR, Seied Amirhossein L, Jadidi A, et al. The effect of novel simple saffron syrup on fatigue reduction in patients with multiple sclerosis. *J Basic Clin Physiol Pharmacol*. 2020;31(6). doi:10.1515/jbcpp-2020-0063
119. Silber MH, Buchfuhrer MJ, Earley CJ, et al. The management of restless legs syndrome: an updated algorithm. *Mayo Clin Proc*. 2021;96(7):1921–1937. doi:10.1016/j.mayocp.2020.12.026
120. Sinniah D. Magnesium deficiency: a possible cause of restless leg syndrome in haemodialysis patients. *Intern Med J*. 2015;45(4):467–468. doi:10.1111/imj.12715
121. Hornyak M, Voderholzer U, Hohagen F, et al. Magnesium therapy for periodic leg movements-related insomnia and restless legs syndrome: an open pilot study. *Sleep*. 1998;21(5):501–505. doi:10.1093/sleep/21.5.501
122. Graber TW, Yee AS, Baker FJ. Magnesium: physiology, clinical disorders, and therapy. *Ann Emerg Med*. 1981;10(1):49–57. doi:10.1016/S0196-0644(81)80461-1
123. Elin RJ. Magnesium: the fifth but forgotten electrolyte. *Am J Clin Pathol*. 1994;102(5):616–622. doi:10.1093/ajcp/102.5.616
124. Neves PD, Graciolli FG, Oliveira IB, et al. Effect of mineral and bone metabolism on restless legs syndrome in hemodialysis patients. *J Clin Sleep Med*. 2017;13(1):89–94. doi:10.5664/jcsm.6396
125. Sanchez-Barcelo EJ, Cos S, Mediavilla D, et al. Melatonin-estrogen interactions in breast cancer. *J Pineal Res*. 2005;38(4):217–222. doi:10.1111/j.1600-079X.2004.00207.x