SYNERGY PUBLISHING PTE. LTD.

Journal of Advances in Medicine Science
https://ojs.bilpublishing.com/index.php/jams

ARTICLE

The Interrelationship Between Sleep Disorders and Memory Impairment: Comorbid Mechanisms and Integrated Treatment Strategies

Yixin Zhang Jing Zhang Na Li*

QingDao Binhai University, Qingdao, Shandong, 266555, China

ARTICLE INFO

Article history
Received: 25 November 2024
Revised: 30 November 2024
Published Online: 16 December 2024

Keywords:
Sleep disorders
Memory impairment
Comorbid Mechanisms
CBT-I

ABSTRACT

Sleep disorders and memory impairments are prevalent in clinical practice and often coexist, significantly impacting individuals' physical, emotional, and cognitive health. The comorbidity between these conditions is multifactorial, involving neurobiological, endocrine, and metabolic factors. Structural brain changes, neuroinflammation, oxidative stress, and neurotransmitter imbalances exacerbate impairments in both sleep and memory function. This paper reviews current combination therapy strategies for managing comorbid sleep and memory disorders, analyzing the effectiveness of pharmacological treatments (such as benzodiazepines and cholinesterase inhibitors) and non-pharmacological interventions (such as Cognitive Behavioral Therapy for Insomnia (CBT-I) and cognitive training). While combination therapies show promising potential, challenges such as drug interactions and patient adherence remain. Future research should focus on exploring underlying mechanisms, developing personalized treatment approaches, and integrating novel therapeutic strategies.

1. Introduction

Sleep disorders (prevalence 8.3% - 45%) like insomnia and OSA, and memory disorders (common in aging) are prevalent and debilitating. Sleep disorders burden physical, emotional, and cognitive health, are linked to comorbidities, and cost healthcare. Memory disorders lead to cognitive decline and dependency. They often coexist (comorbidity). Sleep disturbances can accelerate memory disorder progression; memory loss can disrupt sleep. This bidirectional relationship affects memory consolidation. The comorbidity adds complexity to management. Understanding its mechanisms is key for treatment as untreated cases can cause further deterioration. Integrated therapies may improve outcomes and slow cognitive decline[1-8].

2. Sleep Disorders and Memory Impairments: An Overview

Sleep disorders, such as insomnia, obstructive sleep apnea (OSA), and restless leg syndrome (RLS), are marked by disruptions in the sleep - wake cycle and impact physical and cognitive functions. Insomnia, affecting 10 - 30% globally[9], has three ICSD - 3 categories and is linked to cognitive deficits like memory problems [10,11]. OSA, with a 10 - 20% adult

**Corresponding Author:*
Na Li,
Female, Ph.D., Professor;
Research interests: Neuroscience;
Email: 893981586@qq.com

 DOI: https://doi.org/10.26549/jams.v7i2.22089

prevalence worldwide[12], causes airway obstruction during sleep, leading to hypoxia and sleep fragmentation, and is associated with memory and executive function impairment. RLS (5 - 10% of adults) disrupts sleep and affects cognitive performance[13]. Memory disorders include age - related memory decline, Alzheimer's disease (AD), vascular dementia (VD), etc. Age - related decline is normal but may lead to disease. AD is the main cause of dementia, with progressive memory loss[14,15]. VD is due to cerebrovascular disease and impairs memory and other functions[16].

3. Comorbidity Mechanisms

3.1 Neurobiological Mechanisms

The comorbidity of sleep disorders and memory impairments is closely tied to changes in key brain structures like the hippocampus and prefrontal cortex, which are vital for memory and cognition. In the hippocampus, chronic sleep issues (e.g., from insomnia or obstructive sleep apnea) can cause atrophy[17]. Sleep problems exacerbate neurodegeneration here, harming memory consolidation[18], and are related to increased amyloid - beta deposits, accelerating cognitive decline[19]. The prefrontal cortex, important for executive functions, is also affected. In insomnia and OSA, there are structural changes like reduced gray matter volume[10], creating a cycle of poor sleep and cognitive decline.

3.2 Neurotransmitter Disorders

Sleep disorders and memory impairments are associated with common neurotransmitter system disruptions in neural communication and cognitive processing. The GABAergic system: GABA, the main inhibitory neurotransmitter, regulates sleep and memory. In chronic insomnia, reduced GABAergic function causes excessive neuronal excitability and poor sleep, and impairs hippocampal memory consolidation due to its role in synaptic plasticity[21,22].The glutamatergic system: Glutamate is key for synaptic plasticity, learning, and memory. Insomnia and OSA increase glutamate activity, leading to excitotoxicity, neuronal damage, and memory impairments by disrupting synaptic transmission in relevant brain regions [23].The dopaminergic system: Sleep disorders dysregulate this system, affecting mood and cognition. Dopamine is crucial for attention and working memory. Sleep problems lead to decreased dopamine receptor sensitivity, causing cognitive deficits and attention disorders[24].

3.3 Neuroinflammation and Oxidative Stress

Neuroinflammation and oxidative stress are key in the pathophysiology of comorbid sleep disorders and memory impairments. Sleep disruptions like those from insomnia and OSA trigger brain inflammation via microglia activation and pro - inflammatory cytokine release. Microglia, brain's immune cells, when activated chronically by sleep disturbances, release TNF - α, IL - 1β, and IL - 6[25], impairing neurons and synaptic plasticity in memory - critical regions.Sleep - related issues also increase reactive oxygen species (ROS), causing oxidative stress. This damages cellular components [26,27]. Neuroinflammation and oxidative stress harm synaptic plasticity, crucial for sleep and memory, reducing neural connection strength and disrupting the sleep - cognition balance in relevant brain regions[27].

3.4 Endocrine and Metabolic Mechanisms

Endocrine and metabolic dysfunctions play a significant part in the comorbidity of sleep and memory disorders. Hormonal imbalances disrupt circadian rhythm and memory - related cognitive functions. For instance, melatonin from the pineal gland regulates sleep - wake cycles. In sleep disorders like insomnia and OSA, its secretion may be dysregulated, causing sleep problems and memory deficits as it affects hippocampal function during sleep[28,29]. Cortisol, the stress hormone, also has a diurnal rhythm. In those with chronic sleep disturbances, its dysregulation, like elevated levels at night, can disrupt sleep and memory consolidation, and may lead to hippocampal atrophy and cognitive impairment[29,30].

3.5 Metabolic Disorders

Metabolic dysfunctions, like impaired glucose and lipid metabolism, are closely related to sleep and memory problems. Insulin resistance, where cells respond less to insulin causing high blood glucose, is linked to obesity, type 2 diabetes, and sleep disorders like OSA. It impairs brain energy metabolism in memory - related areas like the hippocampus and prefrontal cortex. It affects glucose transport in neurons, hindering memory consolidation during sleep and synaptic plasticity[31,32]. Dyslipidemia, with abnormal lipid levels, impairs the blood - brain barrier, increasing oxidative stress and inflammation in the brain[33,34], disrupting memory processes.

3.6 Impact on Brain Energy Supply and Neuronal Signaling

Both insulin resistance and dyslipidemia lead to a

DOI: https://doi.org/10.26549/jams.v7i2.22089

shortage of energy supply to neurons. The brain, which is heavily reliant on glucose and lipid metabolism for energy, becomes less efficient in regulating sleep-wake cycles and memory consolidation when metabolic disturbances are present. These disruptions affect not only the brain's energy supply but also neurotransmitter signaling and neuronal plasticity.

3.7 Neurotransmitter Imbalance

Insulin resistance and dyslipidemia also impact neurotransmitter systems, which are critical for sleep regulation and memory function. For instance, insulin resistance has been shown to reduce the activity of neurotransmitters like acetylcholine, which is essential for learning and memory[35]. Furthermore, metabolic dysfunctions lead to an imbalance in excitatory and inhibitory neurotransmitters, such as glutamate and GABA, which are integral for regulating sleep and synaptic plasticity.

In summary, endocrine and metabolic dysfunctions are central to the comorbidity between sleep disorders and memory impairments. Hormonal imbalances such as melatonin and cortisol disruptions interfere with circadian rhythms and memory consolidation, while metabolic disorders, including insulin resistance and dyslipidemia, affect brain energy supply, neuronal signaling, and cognitive function. These mechanisms collectively contribute to the persistence and exacerbation of both sleep and memory disorders, highlighting the need for integrated therapeutic approaches that address both hormonal and metabolic imbalances.

4. Drug Combination Therapy

The treatment of comorbid sleep disorders and memory impairments is complex, as these two conditions are often interlinked, with each exacerbating the other. Drug combination therapy—using pharmacological agents that target both sleep and cognitive dysfunction—has become a promising strategy. The goal is to leverage the synergistic effects of different drug classes to improve both sleep quality and memory function while minimizing side effects. This section focuses on commonly used pharmacological treatments for sleep and memory disorders, as well as the benefits and limitations of these drugs when used alone or in combination.

4.1 Drugs for Sleep Disorders

There are several classes of drugs commonly prescribed to treat sleep disorders, including benzodiazepines, non-benzodiazepine hypnotics, and melatonin receptor agonists. Each of these has a distinct mechanism of action, and their efficacy in managing both sleep and memory dysfunctions varies.

Benzodiazepines: Drugs like lorazepam, temazepam, and diazepam enhance the effects of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter that induces sedative effects. These medications are effective for short-term sleep disturbances, such as insomnia, by reducing neural excitability and promoting relaxation[36]. However, long-term use of benzodiazepines is associated with tolerance, dependence, and cognitive impairment, particularly in elderly patients[37]. Benzodiazepines also interfere with sleep architecture, reducing the proportion of restorative deep sleep and REM sleep, which are crucial for memory consolidation. As a result, while they improve sleep initiation, their effects on memory are counterproductive in the long term.

Non-benzodiazepine Hypnotics: Drugs like zolpidem, eszopiclone, and zaleplon are preferred alternatives to benzodiazepines due to their more selective action on GABA-A receptors, particularly the α1 subunit, which is responsible for sedative effects. These drugs have a shorter half-life, which minimizes their impact on sleep architecture and reduces the risk of cognitive impairment. They are effective in treating insomnia and are considered safer for long-term use compared to benzodiazepines. However, while non-benzodiazepine hypnotics are beneficial for improving sleep onset and maintaining sleep, they do not significantly enhance memory consolidation, and their efficacy in treating memory impairments is limited [36].

Melatonin Receptor Agonists: Melatonin receptor agonists, such as ramelteon, mimic the effects of melatonin, a hormone that regulates the circadian rhythm. These agents promote sleep initiation by acting on the MT1 and MT2 receptors in the suprachiasmatic nucleus of the hypothalamus, which regulates the sleep-wake cycle. Unlike other sleep aids, melatonin receptor agonists do not cause significant cognitive impairment or the risk of dependence, making them suitable for long-term use[38]. However, their effectiveness in treating cognitive impairments, such as memory dysfunction, is limited, and their primary role remains in managing circadian rhythm sleep disorders.

4.2 Drugs for Memory Disorders

Several pharmacological agents are commonly prescribed to treat memory impairments, particularly in conditions like Alzheimer's disease and other forms of dementia. These include cholinesterase inhibitors and NMDA receptor antagonists.

 DOI: https://doi.org/10.26549/jams.v7i2.22089

Cholinesterase Inhibitors: Drugs like donepezil and rivastigmine improve cognitive function in patients with Alzheimer's disease by inhibiting the breakdown of acetylcholine, a neurotransmitter essential for memory and learning. However, these medications have limited efficacy in severe cases and often require long-term use, which can lead to side effects such as gastrointestinal disturbances[39].

NMDA Receptor Antagonists: Memantine, an NMDA receptor antagonist, is used to treat moderate to severe Alzheimer's disease. It works by blocking excessive glutamate activity, which can damage nerve cells. While effective in stabilizing cognitive function for some patients, it does not directly improve sleep, which may limit its benefit in patients with concurrent sleep disorders[40].

While each class of drug—whether for sleep or memory—is effective to some extent, combining sleep-enhancing medications with cognitive enhancers can improve both sleep quality and cognitive function. However, careful consideration of the benefits and risks is necessary, especially in elderly populations where polypharmacy can increase the risk of adverse effects. More research is needed to refine the optimal drug combinations that provide synergistic benefits for both conditions.

4.3 Non-Drug Combination Therapy

The management of comorbid sleep and memory disorders requires a holistic approach that extends beyond pharmacological treatments. Non-drug therapies, such as Cognitive Behavioral Therapy (CBT), sleep hygiene education, and physical therapy, are increasingly recognized for their effectiveness in improving sleep quality and cognitive function. These therapies not only complement pharmacological treatments but also provide long-lasting benefits by addressing the underlying mechanisms of these disorders. This section discusses the principles and methods of applying CBT and sleep hygiene education, as well as the role of physical therapy and rehabilitation training in managing comorbid sleep and memory disorders.

4.4 Cognitive Behavioral Therapy (CBT) and Sleep Hygiene Education

Cognitive Behavioral Therapy for Insomnia (CBT-I) is an evidence-based, non-pharmacological intervention designed to treat insomnia[41]. CBT-I addresses the negative thought patterns and behaviors that contribute to sleep difficulties. The therapy typically includes cognitive restructuring, which helps patients identify and challenge unrealistic beliefs about sleep, and sleep restriction, which encourages a consistent sleep-wake schedule. Studies have shown that CBT-I improves both sleep quality and cognitive performance by promoting more efficient sleep and reducing the negative cognitive consequences of sleep deprivation[42]. CBT-I is particularly effective in patients with comorbid insomnia and cognitive impairment, as it helps break the cycle of sleep disruption and cognitive decline.

In addition to CBT-I, cognitive training is a promising intervention for memory disorders. Cognitive training involves exercises that stimulate various cognitive functions, such as attention, executive function, and memory. These training programs typically use tasks that challenge short-term memory, working memory, and verbal recall, with the aim of improving memory retention and reducing cognitive decline. Recent studies suggest that combining cognitive training with sleep improvement strategies enhances overall cognitive function in patients with memory disorders[9]. Cognitive training and sleep improvement strategies have been shown to improve overall memory performance and delay the progression of cognitive decline in elderly individuals with early-stage memory impairments .

Sleep hygiene education is an essential component of non-drug therapy for sleep and memory disorders. Sleep hygiene involves practices that promote good sleep, such as maintaining a consistent sleep-wake schedule, optimizing the sleep environment (e.g., reducing noise and light exposure), and limiting the consumption of stimulants like caffeine or alcohol. Research has shown that improving sleep hygiene can have significant positive effects on both sleep quality and cognitive function, particularly in individuals with comorbid sleep and memory disorders[43]. By helping patients establish regular sleep habits and optimize their sleep environment, sleep hygiene education can complement the effects of CBT and other cognitive interventions.

4.5 Physical Therapy and Rehabilitation Training

Physical therapy, including methods like light therapy and transcranial magnetic stimulation (TMS), plays a role in improving sleep and memory function in patients with comorbid sleep and memory disorders[44]. Light therapy has been shown to regulate circadian rhythms, improving both sleep quality and cognitive function in individuals with disrupted sleep-wake cycles[45]. Transcranial magnetic stimulation (TMS), which involves the application of magnetic fields to stimulate brain regions, has been shown to enhance cognitive performance and alleviate symptoms

DOI: https://doi.org/10.26549/jams.v7i2.22089

of sleep disorders[46]. TMS, when used in combination with other therapies, may enhance memory consolidation and improve sleep in patients with comorbid conditions.

Rehabilitation training, such as exercise therapy and memory rehabilitation training, also plays an important role in managing comorbid sleep and memory disorders. Regular physical exercise has been shown to improve both sleep quality and memory function, particularly in older adults[46]. Exercise improves brain plasticity, enhances hippocampal function, and promotes neurogenesis, which benefits both sleep regulation and cognitive function. In combination with cognitive training and sleep hygiene education, exercise therapy may provide a comprehensive approach to improving both physical and cognitive health in individuals with comorbid sleep and memory impairments.

5. Conclusion and Prospect

Recent research has unveiled a complex, multi-factorial relationship between sleep disorders and memory impairments, highlighting that the comorbidity between these conditions is driven by a variety of overlapping mechanisms. The key findings point to neurobiological changes, including structural alterations in the hippocampus and prefrontal cortex, regions that are crucial for both sleep regulation and memory function. Studies have shown that neurodegeneration in these areas contributes to impaired sleep and memory consolidation. These structural changes, along with disrupted neural connectivity, impair memory consolidation processes during sleep and compromise overall cognitive function.

In addition to structural changes, neuroinflammation and oxidative stress are emerging as significant contributors to the comorbidity. The activation of microglia and the subsequent release of pro-inflammatory cytokines disrupt normal synaptic plasticity, leading to cognitive impairments and sleep disturbances. These factors increase the vulnerability of neurons to damage, further exacerbating both sleep and memory dysfunction. Moreover, neurotransmitter imbalances, particularly in GABA, serotonin, and dopamine pathways, play a critical role in this interaction. These neurotransmitters are essential for regulating sleep-wake cycles, and disturbances in their signaling exacerbate both sleep disorders and memory dysfunction.

Endocrine imbalances, particularly in melatonin and cortisol, further contribute to the comorbidity. Melatonin, a hormone critical for sleep regulation, is often found at abnormal levels in patients with sleep disorders, impairing the sleep-wake cycle. Elevated cortisol levels, commonly seen in individuals with chronic stress or sleep disturbances, disrupt sleep architecture, exacerbate cognitive decline, and further impair memory consolidation. Furthermore, recent studies have also pointed to the dysregulation of neurotrophic factors such as brain-derived neurotrophic factor (BDNF), which is essential for synaptic plasticity and cognitive function.

Combination therapy, which involves the use of both pharmacological and non-pharmacological treatments, is increasingly seen as a promising approach for managing comorbid sleep and memory disorders. Pharmacological treatments, such as benzodiazepines, non-benzodiazepine hypnotics, and cholinesterase inhibitors, have demonstrated efficacy in alleviating the symptoms of sleep and memory dysfunction. However, their effectiveness is often limited by side effects, including cognitive impairment, dependency, and tolerance. Non-pharmacological treatments, such as Cognitive Behavioral Therapy for Insomnia (CBT-I) and cognitive training, have gained significant attention for their ability to treat the root causes of these disorders without the side effects associated with medications. CBT-I, for instance, addresses the negative thoughts and behaviors that perpetuate insomnia, while cognitive training aims to enhance cognitive function in patients with memory impairments[47]. These therapies have shown strong evidence of improving both sleep and cognitive function.

While the combination of drug therapies with CBT-I or cognitive training has shown promising results, challenges remain. For instance, potential drug interactions can complicate treatment regimens, and patient adherence to non-drug therapies remains a significant barrier. Moreover, the integration of pharmacological and psychological approaches requires careful consideration to ensure both safety and efficacy.

Moving forward, several key research areas must be addressed to improve the management of comorbid sleep disorders and memory impairments. First, further exploration of the underlying mechanisms of comorbidity is crucial to develop targeted therapies that can address both conditions simultaneously. More studies are needed to understand the synergistic effects of neuroinflammation, neurotransmitter imbalances, and metabolic disruptions in these disorders.

In addition, the development of personalized medicine is essential. Genetic, environmental, and individual factors must be considered to tailor treatments to each patient's unique needs, optimizing therapeutic outcomes. Finally, future research should focus on novel treatment strategies, including more advanced drug combinations and innovative non-pharmacological treatments, such as brain stimulation therapies and digital health interventions. By

 DOI: https://doi.org/10.26549/jams.v7i2.22089

advancing our understanding of these mechanisms and improving treatment modalities, the long-term prognosis for patients with comorbid sleep and memory disorders can be significantly enhanced.

References

[1] Qiu, D., Yu, Y., Li, R.-Q., Li, Y.-L., & Xiao, S.-Y. (2020). Prevalence of sleep disturbances in Chinese healthcare professionals: A systematic review and meta-analysis. Sleep Medicine, 67, 258–266. https://doi.org/10.1016/j.sleep.2019.01.047

[2] Wang, J., Wu, J., Liu, J., Meng, Y., Li, J., Zhou, P., Xu, M., Yan, Q., Li, Q., Yin, X., & Gong, Y. (2023). Prevalence of sleep disturbances and associated factors among Chinese residents: A web-based empirical survey of 2019. Journal of Global Health, 13, 04071. https://doi.org/10.7189/jogh.13.04071

[3] Stranges, S., Tigbe, W., Gómez-Olivé, F. X., Thorogood, M., & Kandala, N.-B. (2012). Sleep Problems: An Emerging Global Epidemic? Findings From the INDEPTH WHO-SAGE Study Among More Than 40,000 Older Adults From 8 Countries Across Africa and Asia. Sleep, 35(8), 1173–1181. https://doi.org/10.5665/sleep.2012

[4] Mo, W., Liu, X., Yamakawa, M., Koujiya, E., Takeya, Y., Shigenobu, K., Adachi, H., & Ikeda, M. (2024). Prevalence of sleep disturbances in people with mild cognitive impairment: A systematic review and meta-analysis. Psychiatry Research, 339, 116067. https://doi.org/10.1016/j.psychres.2024.116067

[5] Guan, Q., Hu, X., Ma, N., He, H., Duan, F., Li, X., Luo, Y., & Zhang, H. (2020). Sleep Quality, Depression, and Cognitive Function in Non-Demented Older Adults. Journal of Alzheimer's Disease, 76(4), 1637–1650. https://doi.org/10.3233/JAD-190990

[6] Hernandez, C., & Shukla, S. (2022). Liposome based drug delivery as a potential treatment option for Alzheimer's disease. Neural Regeneration Research, 17(6), 1190. https://doi.org/10.4103/1673-5374.327328

[7] Shi, L., Chen, S.-J., Ma, M.-Y., Bao, Y.-P., Han, Y., Wang, Y.-M., Shi, J., Vitiello, M. V., & Lu, L. (2018). Sleep disturbances increase the risk of dementia: A systematic review and meta-analysis. Sleep Medicine Reviews, 40, 4–16. https://doi.org/10.1016/j.smrv.2017.06.010

[8] Xu, W., Tan, C.-C., Zou, J.-J., Cao, X.-P., & Tan, L. (2020). Sleep problems and risk of all-cause cognitive decline or dementia: An updated systematic review and meta-analysis. Journal of Neurology, Neurosurgery & Psychiatry, 91(3), 236–244. https://doi.org/10.1136/jnnp-2019-321896

[9] Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, Espie CA, Garcia-Borreguero D, Gjerstad M, Gonçalves M, Hertenstein E, Jansson-Fröjmark M, Jennum PJ, Leger D, Nissen C, Parrino L, Paunio T, Pevernagie D, Verbraecken J, Weeß HG, Wichniak A, Zavalko I, Arnardottir ES, Deleanu OC, Strazisar B, Zoetmulder M, Spiegelhalder K. European guideline for the diagnosis and treatment of insomnia. J Sleep Res. 2017 Dec;26(6):675-700. doi: 10.1111/jsr.12594.

[10] Davidescu, D., Galea-Holhoș, L. B., Voiță-Mekereș, F., & Davidescu, L. (2023). Effects of Sleep Deprivation on Learning and Memory: A Review Study. Journal of Biochemical Technology, 14(4), 25–30. https://doi.org/10.51847/01ztnjmk66

[11] Casagrande, M., Forte, G., Favieri, F., Corbo, I., 2022. Sleep quality and aging: a systematic review on healthy older people, mild cognitive impairment and Alzheimer's disease. Int. J. Environ. Res. Public Health 19 (14), 8457.

[12] Kirsch DB. Obstructive Sleep Apnea. Continuum (Minneap Minn). 2020 Aug;26(4):908-928. doi: 10.1212/CON.0000000000000885.

[13] Gossard TR, Trotti LM, Videnovic A, St Louis EK. Restless Legs Syndrome: Contemporary Diagnosis and Treatment. Neurotherapeutics. 2021 Jan;18(1):140-155. doi:10.1007/s13311-021-01019-4.

[14] Müller S, Mychajliw C, Reichert C, Melcher T, Leyhe T. Autobiographical Memory Performance in Alzheimer's Disease Depends on Retrieval Frequency. J Alzheimers Dis. 2016 Apr 18;52(4):1215-25. doi: 10.3233/JAD-151071.

[15] El Haj M, Colombel F, Kapogiannis D, Gallouj K. False Memory in Alzheimer's Disease. Behav Neurol. 2020 Feb 19;2020:5284504. doi: 10.1155/2020/5284504.

[16] Chang Wong E, Chang Chui H. Vascular Cognitive Impairment and Dementia. Continuum (Minneap Minn). 2022 Jun 1;28(3):750-780. doi: 10.1212/CON.0000000000001124.

[17] Prabhakar NR, Peng YJ, Nanduri J. Hypoxia-inducible factors and obstructive sleep apnea. J Clin Invest. 2020 Oct 1;130(10):5042-5051. doi: 10.1172/JCI137560.

[18] Semenza GL, Prabhakar NR. The role of hypoxia-inducible factors in carotid body (patho) physiology. J Physiol. 2018 Aug;596(15):2977-2983. doi: 10.1113/JP275696.

[19] Shokri-Kojori E, Wang GJ, Wiers CE, Demiral SB,

DOI: https://doi.org/10.26549/jams.v7i2.22089

Guo M, Kim SW, Lindgren E, Ramirez V, Zehra A, Freeman C, Miller G, Manza P, Srivastava T, De Santi S, Tomasi D, Benveniste H, Volkow ND. β-Amyloid accumulation in the human brain after one night of sleep deprivation. Proc Natl Acad Sci U S A. 2018 Apr 24;115(17):4483-4488.
doi: 10.1073/pnas.1721694115.

[20] Mingming Z, Wenhong C, Xiaoying M, Yang J, Liu HH, Lingli S, Hongwu M, Zhirong J. Abnormal prefrontal functional network in adult obstructive sleep apnea: A resting-state fNIRS study. J Sleep Res. 2024 Apr;33(2):e14033.
doi: 10.1111/jsr.14033.

[21] Li J, Chen L, Guo F, Han X. The Effects of GABAergic System under Cerebral Ischemia: Spotlight on Cognitive Function. Neural Plast. 2020 Sep 28;2020:8856722.
doi: 10.1155/2020/8856722.

[22] Varinthra P, Anwar SNMN, Shih SC, Liu IY. The role of the GABAergic system on insomnia. Tzu Chi Med J. 2024 Mar 26;36(2):103-109.
doi: 10.4103/tcmj.tcmj_243_23.

[23] Dresp-Langley B, Hutt A. Digital Addiction and Sleep. Int J Environ Res Public Health. 2022 Jun 5;19(11):6910.
doi: 10.3390/ijerph19116910.

[24] Ugalde-Muñiz P, Hernández-Luna MG, García-Velasco S, Lugo-Huitrón R, Murcia-Ramírez J, Martínez-Tapia RJ, Noriega-Navarro R, Navarro L. Activation of dopamine D2 receptors attenuates neuroinflammation and ameliorates the memory impairment induced by rapid eye movement sleep deprivation in a murine model. Front Neurosci. 2022 Oct 5;16:988167.
doi: 10.3389/fnins.2022.988167.

[25] Ling J, Li B, Yuan X, Yang W, Sun K. Intermittent Hypoxia Impairs Cognitive Function and Promotes Mitophagy and Lysophagy in Obstructive Sleep Apnea-Hypopnea Syndrome Rat Model. Mol Biotechnol. 2024 Nov 16.
doi: 10.1007/s12033-024-01319-y.

[26] Lv R, Liu X, Zhang Y, Dong N, Wang X, He Y, Yue H, Yin Q. Pathophysiological mechanisms and therapeutic approaches in obstructive sleep apnea syndrome. Signal Transduct Target Ther. 2023 May 25;8(1):218.
doi: 10.1038/s41392-023-01496-3.

[27] Terzi A, Ngo KJ, Mourrain P. Phylogenetic conservation of the interdependent homeostatic relationship of sleep regulation and redox metabolism. J Comp Physiol B. 2024 Jun;194(3):241-252.
doi: 10.1007/s00360-023-01530-4.

[28] Poza JJ, Pujol M, Ortega-Albás JJ, Romero O; Insomnia Study Group of the Spanish Sleep Society (SES). Melatonin in sleep disorders. Neurologia (Engl Ed). 2022 Sep;37(7):575-585.
doi: 10.1016/j.nrleng.2018.08.004.

[29] Nogueira HA, de Castro CT, da Silva DCG, Pereira M. Melatonin for sleep disorders in people with autism: Systematic review and meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry. 2023 Apr 20;123:110695.
doi: 10.1016/j.pnpbp.2022.110695.

[30] Bin Ibrahim MZ, Benoy A, Sajikumar S. Long-term plasticity in the hippocampus: maintaining within and 'tagging' between synapses. FEBS J. 2022 Apr;289(8):2176-2201.
doi: 10.1111/febs.16065.

[31] Reutrakul S, Van Cauter E. Sleep influences on obesity, insulin resistance, and risk of type 2 diabetes. Metabolism. 2018 Jul;84:56-66.
doi: 10.1016/j.metabol.2018.02.010.

[32] Wang J, Li L, Zhang Z, Zhang X, Zhu Y, Zhang C, Bi Y. Extracellular vesicles mediate the communication of adipose tissue with brain and promote cognitive impairment associated with insulin resistance. Cell Metab. 2022 Sep 6;34(9):1264-1279.e8.
doi: 10.1016/j.cmet.2022.08.004.

[33] Adedayo AM, Olafiranye O, Smith D, Hill A, Zizi F, Brown C, Jean-Louis G. Obstructive sleep apnea and dyslipidemia: evidence and underlying mechanism. Sleep Breath. 2014 Mar;18(1):13-8.
doi: 10.1007/s11325-012-0760-9.

[34] Bonsignore MR. Obesity and Obstructive Sleep Apnea. Handb Exp Pharmacol. 2022;274:181-201.
doi: 10.1007/164_2021_558.

[35] Du L, Yang D, Wu L, Mei L, Wu S, Ba Y, Bao Y, Su R, Song L. Integration of Gut Microbiota, Serum Metabolomic, and Network Pharmacology to Reveal the Anti Insomnia Mechanism of Mongolian Medicine Sugemule-4 Decoction on Insomnia Model Rats. Drug Des Devel Ther. 2024 Jun 27;18:2617-2639.
doi: 10.2147/DDDT.S455600.

[36] de Mendonça FMR, de Mendonça GPRR, Souza LC, Galvão LP, Paiva HS, de Azevedo Marques Périco C, Torales J, Ventriglio A, Castaldelli-Maia JM, Sousa Martins Silva A. Benzodiazepines and Sleep Architecture: A Systematic Review. CNS Neurol Disord Drug Targets. 2023;22(2):172-179.
doi: 10.2174/1871527320666210618103344.

[37] Wright A, Diebold J, Otal J, Stoneman C, Wong J, Wallace C, Duffett M. The Effect of Melatonin on Benzodiazepine Discontinuation and Sleep Quality in Adults Attempting to Discontinue Benzodiazepines:

A Systematic Review and Meta-Analysis. Drugs Aging. 2015 Dec;32(12):1009-18.
doi: 10.1007/s40266-015-0322-5.

[38] Riemann D, Espie CA, Altena E, Arnardottir ES, Baglioni C, Bassetti CLA, Bastien C, Berzina N, Bjorvatn B, Dikeos D, Dolenc Groselj L, Ellis JG, Garcia-Borreguero D, Geoffroy PA, Gjerstad M, Gonçalves M, Hertenstein E, Hoedlmoser K, Hion T, Holzinger B, Janku K, Jansson-Fröjmark M, Järnefelt H, Jernelöv S, Jennum PJ, Khachatryan S, Krone L, Kyle SD, Lancee J, Leger D, Lupusor A, Marques DR, Nissen C, Palagini L, Paunio T, Perogamvros L, Pevernagie D, Schabus M, Shochat T, Szentkiralyi A, Van Someren E, van Straten A, Wichniak A, Verbraecken J, Spiegelhalder K. The European Insomnia Guideline: An update on the diagnosis and treatment of insomnia 2023. J Sleep Res. 2023 Dec;32(6):e14035.
doi: 10.1111/jsr.14035.

[39] Zhang H, Wang Y, Wang Y, Li X, Wang S, Wang Z. Recent advance on carbamate-based cholinesterase inhibitors as potential multifunctional agents against Alzheimer's disease. Eur J Med Chem. 2022 Oct 5;240:114606.
doi: 10.1016/j.ejmech.2022.114606.

[40] Rana V, Ghosh S, Bhatt A, Bisht D, Joshi G, Purohit P. N-Methyl-D-Aspartate (NMDA) Receptor Antagonists and their Pharmacological Implication: A Medicinal Chemistry-oriented Perspective Outline. Curr Med Chem. 2024;31(29):4725-4744.
doi: 10.2174/0109298673288031240405061759.

[41] Perlis ML, Posner D, Riemann D, Bastien CH, Teel J, Thase M. Insomnia. Lancet. 2022 Sep 24;400(10357):1047-1060.
doi: 10.1016/S0140-6736(22)00879-0.

[42] Dewald-Kaufmann J, de Bruin E, Michael G. Cognitive Behavioral Therapy for Insomnia (CBT-i) in School-Aged Children and Adolescents. Sleep Med Clin. 2019 Jun;14(2):155-165.
doi: 10.1016/j.jsmc.2019.02.002.

[43] Chung KF, Lee CT, Yeung WF, Chan MS, Chung EW, Lin WL. Sleep hygiene education as a treatment of insomnia: a systematic review and meta-analysis. Fam Pract. 2018 Jul 23;35(4):365-375.
doi: 10.1093/fampra/cmx122.

[44] Holbert RC, Carr BR, Bussing R. An open label pilot trial of sequential bifrontal low frequency r-TMS in the treatment of primary insomnia. Psychiatry Res. 2023 Jun;324:115194.
doi: 10.1016/j.psychres.2023.115194.

[45] Centorino MB, Bajor LA, Gootam PK, Nakase-Richardson R, Kozel FA. The Relationship of Transcranial Magnetic Stimulation With Sleep and Plasticity. J Psychiatr Pract. 2020 Nov;26(6):434-443.
doi: 10.1097/PRA.0000000000000506.

[46] Kweon J, Fukuda AM, Gobin AP, Haq L, Carpenter LL, Brown JC. Effect of sleep quality on repetitive transcranial magnetic stimulation outcomes in depression. Front Psychiatry. 2024 Sep 23;15:1458696.
doi: 10.3389/fpsyt.2024.1458696.

[47] Ballesio A, Bacaro V, Vacca M, Chirico A, Lucidi F, Riemann D, Baglioni C, Lombardo C. Does cognitive behaviour therapy for insomnia reduce repetitive negative thinking and sleep-related worry beliefs? A systematic review and meta-analysis. Sleep Med Rev. 2021 Feb;55:101378.
doi: 10.1016/j.smrv.2020.101378.

DOI: https://doi.org/10.26549/jams.v7i2.22089