Biomedical Research Bulletin. 2025;3(2):72-76
doi: 10.34172/biomedrb.9069
http://biomedrb.com

Review Article

Sleep, Glymphatic Flow, and Proteostasis: Linking Sleep Physiology to Neurodegenerative Risk

Leila Hosseini[1*], Ali Reza Shafiee-Kandjani[1], Mojtaba Ziaee[2], Vida Mafikandi[3], Nasrin Abolhasanpour[4]

[1]Research Center of Psychiatry and Behavioral Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Medicinal Plants Research Center, Maragheh Faculty of Medical Sciences, Maragheh, Iran
[3]Neurosciences Research Center (NSRC), Tabriz University of Medical Sciences, Tabriz, Iran
[4]Research Center for Evidence-Based Medicine, Iranian EBM Center: A Joanna Briggs Institute (JBI) Center of Excellence, Tabriz University of Medical Sciences, Tabriz, Iran

Article History:
Received: May 30, 2025
Revised: June 5, 2025
Accepted: June 15, 2025
ePublished: June 30, 2025

***Corresponding Author:**
Leila Hosseini,
Email: leilahosseini337@gmail.com

Abstract
Sleep is essential for maintaining brain health, cognitive performance, and neurological function. Accordingly, increasing scientific attention has recently been directed toward understanding the physiological mechanisms through which sleep exerts its restorative effects. The discovery of the glymphatic system (GS) provides a new conceptual framework for understanding how the brain eliminates metabolic waste and neurotoxic aggregates. During sleep, GS facilitates the convective exchange of cerebrospinal and interstitial fluids in order to remove harmful byproducts. These processes are linked to proteostasis, the regulation of protein synthesis, folding, and degradation, ensuring cellular homeostasis and preventing the accumulation of misfolded proteins. The dysfunction of glymphatic flow or proteostasis significantly contributes to the onset and progression of neurodegenerative diseases. According to research findings, poor sleep quality and short sleep duration produce decreased glymphatic clearance of debris, contributing to protein aggregation and cellular die-off and injury. Conversely, restorative sleep impairs waste flushing while protecting neural function. The present review provides findings related to recent research about the interplay of sleep physiology, glymphatic flow, and proteostasis to simultaneously provide an understanding of these three interrelated processes in the context of risk of neurodegenerative disease. Moreover, it presents emerging treatment approaches, such as sleep optimization, pharmacological modulation of glymphatic flow, and enhancement of proteostasis pathways that may avoid age-related cognitive decline that ultimately plays a role in brain health across the lifespan.
Keywords: Sleep, Glymphatic system, Proteostasis, Neurodegeneration

Introduction

Sleep is a vital physiological process, which is vital not only for restoring energy and supporting synaptic plasticity but also for maintaining metabolic, immune, and cognitive balance.[1] Epidemiological studies consistently associate poor sleep quality, reduced slow-wave sleep (SWS), and fragmented sleep with a higher risk of neurodegenerative disorders, including Alzheimer's disease (AD) and Parkinson's disease (PD).[2] The mechanisms behind this connection remained unclear for many years. Nonetheless, the recent discovery of the glymphatic system (GS), a glial-assisted waste clearance network in the brain, provides a compelling mechanistic pathway connecting sleep physiology to neural proteostasis and neurodegenerative risk.[3]

Proteostasis refers to the maintenance of proper protein synthesis, folding, trafficking, and degradation. This process is essential in neurons, which are long-lived and metabolically active. When proteostasis is disrupted, misfolded and aggregated proteins, such as amyloid-β (Aβ), tau, and α-synuclein, accumulate. These features are the hallmarks of a variety of neurodegenerative diseases.[4] The interaction between sleep, glymphatic clearance, and proteostasis creates an integrated network. This network may explain how chronic sleep dysfunction contributes to neurodegeneration.[4] This review integrates current knowledge on (i) sleep architecture and its role in brain clearance, (ii) the regulatory mechanisms of the GS, and (iii) intracellular proteostasis pathways in the brain. It further examines (iv) evidence of the interplay among these three systems in neurodegenerative diseases and (v) therapeutic implications and future directions. By connecting these topics, this study aims to clarify how sleep physiology influences glymphatic and proteostatic processes, how their disruption can increase neurodegenerative risk, and where research and interventions might focus in the

coming years.

Sleep Physiology and Brain Clearance

Sleep is conventionally divided into rapid eye movement (REM) and non-REM (NREM) stages, with NREM further categorized into N1, N2, and N3 (also termed SWS). SWS features high-amplitude delta waves, synchronous cortical activity, reduced neuronal firing and metabolic demand, and increased interstitial space volume.[1] This state appears particularly conducive to brain clearance; studies indicate that the extracellular space (ECS) volume increases approximately 60% during SWS, thereby reducing resistance to interstitial fluid (ISF) flow.[5] SWS is generally regarded as the most restorative phase of sleep and is closely linked to sleep quality and maintenance; nevertheless, its specific functions and their consequences for daytime functioning are not fully elucidated yet.[6] Chronic sleep deficits are associated with impairments in cognition and memory, and current evidence demonstrates a link between reduced SWS and various clinical and psychiatric disorders. Enhancing sleep architecture by increasing SWS, regardless of changes in total sleep duration, may improve these related conditions. Continued research and the development of innovative pharmacological and non-pharmacological sleep therapies are warranted.[7] According to multiple animal studies, the influx of cerebrospinal fluid (CSF) into the brain parenchyma and its exchange with ISF significantly increase during sleep or anesthesia compared to wakefulness. For example, tracer research on mice reported approximately a 2-fold higher clearance of Aβ during sleep.[8] Recent human neuroimaging studies employing diffusion tensor imaging along perivascular spaces have shown that individuals with poor sleep quality exhibit lower ALPS indices, suggesting reduced glymphatic clearance capacity.[9]

Chronic sleep deprivation or fragmentation directly impairs these clearance processes. In animal models, even one night of sleep deprivation rapidly increases hippocampal Aβ deposition and slows tracer egress.[10] Similarly, human studies indicate that short sleep duration (< 6 h) or disrupted SWS correlates with elevated CSF Aβ/tau and greater amyloid positron emission tomography. Mechanistically, wakefulness is associated with elevated norepinephrine levels, which constrict the ECS and suppress perivascular fluid movement, thereby reducing glymphatic flux.[11]

Thus, high-quality sleep, particularly with robust SWS, appears to offer greater brain clearance potential via an enlarged ECS and enhanced CSF-ISF exchange. Conversely, sleep disruption leads to decreased clearance and increased risk for protein accumulation. Accordingly, a comprehensive exploration of the GS is essential.

Glymphatic System: Function and Regulators of Glymphatic Flow

The GS is a brain-specific fluid clearance network in which CSF enters along periarterial channels, exchanges with ISF via astrocyte-expressed aquaporin-4 (AQP4) water channels at the end feet, and exits along perivenous or meningeal lymphatic routes.[12] Astrocytes are responsible for the formation of perivascular tunnels, which are instrumental in promoting convective fluid transport. Moreover, the polarized expression of AQP4 on the end-feet of astrocytes is crucial for the efficacy of fluid exchange; any disruption of this polarization significantly impairs the clearance process.[13] The GS is a waste-clearance system that uses perivascular tunnels to remove soluble proteins and metabolites from the CNS, facilitates the distribution of compounds throughout the brain, and primarily functions during sleep. In addition, it is involved in the removal of neurotoxic waste products, and its dysfunction may be associated with the pathogenesis of neurodegenerative diseases, cerebral trauma, and stroke.[3] The GS exhibits a decline in function with aging. According to research, older adults show lower DTI-ALPS indices, reduced tracer influx, and increased perivascular space (PVS) dilation.[14] These changes coincide with increased Aβ accumulation in the aging brain. Furthermore, pathological conditions (e.g., AD and PD) are linked to even greater impairments in glymphatic flow and changes in the distribution of AQP4 channels.[2]

Several factors modulate glymphatic efficacy:

- Sleep state: As noted, SWS enhances glymphatic flow. It has been demonstrated that glymphatic influx is associated with delta wave power and is the highest during deep NREM sleep. [15]
- Arterial pulsatility: The driving force for periarterial CSF influx is, in part, the pulsatile dilation of arteries. Aging and hypertension reduce arterial compliance and dampen pulsatile amplitude, leading to less glymphatic flow.[16]
- Vascular and astrocytic integrity: Impaired clearance is also related to age-related stiffening of the vasculature, astrocytic reactivity, and loss of AQP4 polarization. [17]
- Body posture: Interestingly, in rodent models, lateral asleep positioning increases glymphatic clearance vs. prone or supine positions. [18]

Proteostasis in the Brain

Influence of Sleep on Proteostasis

Proteostasis is the maintenance of the proteome through coordinated regulation of protein synthesis, chaperone-mediated folding, post-translational modifications, trafficking, and degradation via the ubiquitin-proteasome system and autophagy–lysosomal pathways.[19] In post-mitotic, long-lived neurons, robust proteostasis is essential for preventing the accumulation of misfolded or aggregated proteins and maintaining synaptic and metabolic functions.[20] Recent findings suggest that sleep plays a supportive role in proteostatic mechanisms. For

instance, studies in animal models demonstrate that sleep enhances the expression of molecular chaperones and increases autophagic flux in brain tissue. In contrast, sleep deprivation reduces autophagy markers, causes the accumulation of ubiquitinated proteins, and increases endoplasmic reticulum stress. Overall, these perturbations may impair the degradation of Aβ, tau, α-synuclein, and other aggregation-prone proteins.[21] Ortiz-Vega et al found that sleep modulation plays a critical role in maintaining proteostasis and mitigating neurodegeneration in Drosophila models of tauopathy. Research also shows that sleep deprivation worsens neurodegenerative outcomes, whereas inducing sleep has a beneficial effect by enhancing autophagy and decreasing the accumulation of toxic tau proteins.[22]

Proteostasis and Aging

Proteostasis functions at the intracellular level, thereby facilitating the removal of misfolded proteins. However, the GS is responsible for the clearance of extracellular solutes and interstitial aggregates.[23] Thus, efficient clearance requires the impairment of both systems; impairment of either may result in the buildup of toxic proteins. According to evidence, disruptions in glymphatic flow exacerbate proteostatic stress and vice versa.[24]

With advanced age, the proteostasis capacity reduces, as indicated by a decline in autophagy efficiency, a decrease in chaperone expression and proteasome activity, as well as an increase in oxidative damage.[25] These modifications facilitate the aggregation of Aβ, tau, and α-synuclein, a phenomenon that is further exacerbated by compromised glymphatic clearance.[26] The deficiency of AQP4 disrupts clearance mechanisms in AD models, leading to failures in proteostasis and dysfunction within neuronal circuits. Proteostasis acts as an essential intracellular defense mechanism against the aggregation of proteins, with its effectiveness augmented during sleep and adversely affected by aging and sleep disturbances. The interplay between proteostasis and glymphatic clearance suggests that the simultaneous dysfunction of these systems may signify a credible mechanistic pathway for the inception of neurodegenerative diseases.[27]

Interplay Between Sleep, Glymphatic Flow, and Neurodegeneration

In AD, hallmark pathologies include Aβ plaques and tau neurofibrillary tangles. Evidence shows that reductions in SWS and sleep fragmentation precede cognitive deficits and link with increased amyloid burden.[28] Neuroimaging studies have associated a lower ALPS index (impaired glymphatic flow) with greater Aβ deposition and cognitive decline.[29] In transgenic mouse models, the lack of AQP4 polarization results in a 25%–50% increase in Aβ accumulation despite unchanged production rates.[30]

Sleep disorders, especially REM-sleep behavior disorder, often appear early in prodromal PD. Recent studies have reported that patients with PD have reduced glymphatic function and greater PVS burden.[31,32] α-synuclein clearance may depend on glymphatic flow; AQP4 deficiency has been involved in the acceleration of α-synuclein aggregation and dopaminergic neuron loss, which are the main pathological features of PD.[33] Similar mechanisms are proposed for other neurodegenerative conditions (e.g., Huntington's disease and amyotrophic lateral sclerosis), where protein clearance and sleep disturbances are present.[34]

Therapeutic Implications

Sleep Optimization Interventions

Enhancing the quality and quantity of sleep, particularly by increasing SWS, represents a primary avenue for intervention aimed at promoting cerebral clearance via the GS and augmenting protein homeostasis. Recent studies indicate that electrical or acoustic slow-oscillation stimulation during sleep can potentially amplify SWS power, subsequently leading to improved clearance of accumulated metabolites and proteins.[35] For instance, research demonstrated that sensory stimulation (e.g., low-frequency acoustic) or transcranial stimulation during sleep may bolster CSF and ISF flow.[36] Additionally, behavioral interventions have been proposed, including stabilizing sleep timing, reducing sleep fragmentation, managing sleep apnea, and optimizing sleep posture (e.g., sleeping laterally).[37] It has been demonstrated that the lateral sleeping position is related to increased glymphatic efficiency compared to the supine (on the back) or prone (on the stomach) positions.[38]

Targeting Glymphatic Function Directly

Beyond optimizing sleep, several interventions are being explored to directly enhance GS function:

1. Modulation of AQP4 channels: Preclinical studies have revealed that decreased AQP4 expression or the loss of its polarity on astrocytic endfeet is associated with diminished CSF/ISF flow and increased Aβ accumulation. [39] Therefore, pharmacological agents capable of regulating AQP4 or restoring its polarization are a key focus of research.[40]
2. Augmenting arterial pulsation/enhancing vascular function: Considering that arterial pulsation is considered one of the primary driving forces for fluid flow within the PVS, improving vascular health (e.g., through exercise, blood pressure reduction, and mitigation of atherosclerosis) is posited to enhance glymphatic performance. This approach directly addresses the mechanical propulsion required for efficient glymphatic clearance.[41]
3. Imaging and monitoring of glymphatic function: The use of imaging techniques (e.g., tracer-based magnetic resonance imaging, the ALPS index, and other advanced methodologies) is emerging for the early detection of impaired glymphatic function,

even before the onset of clinical symptoms. These diagnostic tools are vital for facilitating the design of future *preventive* interventions.[42]

Combined Interventions and Precision Approaches

Given the complex interplay among sleep, the GS, and proteostasis, a combination of multiple interventions that simultaneously improve sleep, augment clearance flow, and boost cellular protein-elimination capacity may yield the maximum effect. A comprehensive strategy for reducing the risk of neurodegeneration in high-risk individuals might involve combining behavioral sleep therapy with regular exercise and an astrocyte/AQP4-modulating pharmacological agent.[43] Moreover, personalized strategies are critical; people should be selected based on specific risk indicators (e.g., age, APOE4 genotype, baseline ALPS function index, and sleep quality) and then assigned targeted interventions.[44] Eventually, the use of biomarkers, advanced imaging, and pre-intervention or post-intervention assessments can help quantify and validate the effectiveness of these combined approaches.

Conclusion

Evidence suggests that the interrelationship between sleep, the GS, and proteostasis is essential for sustaining nervous system homeostasis. Adequate and high-quality sleep, particularly the enhancement of SWS, optimizes glymphatic clearance, while vascular integrity and astrocytic AQP4 polarization modulate this process. In addition to intracellular proteostasis pathways, these mechanisms form an integrated defense against neurotoxic protein accumulation. However, impairments in any of these systems may shorten the onset and/or progression of neurodegenerative diseases. Consequently, multi-modal interventions, including the regulation of sleep behaviors to improve sleep and sleep physiology with exercise (i.e., regular aerobic training) to maintain vascular health and modulation of astrocyte reflection or AQP4 with pharmacology, are potential protective strategies to target neurodegeneration. It is recommended that future research focus on longitudinal human studies, the use of standardized imaging biomarkers, and mechanistic studies to support clinical application, further validating the potential of the sleep-glymphatic-alterations in the proteostasis framework. This study, therefore, identified significant opportunities on the frontiers of the prevention and treatment of neurodegenerative disorders.

Authors' Contribution

Conceptualization: Mojtaba Ziaee and Leila Hosseini.
Data curation: Leila Hosseini.
Formal analysis: Leila Hosseini.
Investigation: Leila Hosseini and Vida Mafikamdi.
Methodology: Leila Hosseini and Vida Mafikamdi.
Project administration: Leila Hosseini and Vida Mafikandi.
Resources: Vida Mafikandi and Ali Reza Shafiee-Kandjani.
Supervision: Leila Hosseini.
Validation: Leila Hosseini.
Writing–original draft: Leila Hosseini and Vida Mafikandi.
Writing–review and editing: Mojtaba Ziaee, Leila Hosseini, Vida Mafikandi, Ali Reza Shafiee-Kandjani, and Nasrin Abolhasanpour.

Competing Interests

None.

Ethical Approval

Not applicable.

Funding

The authors received no financial support.

References

1. Pathmanathan J, Westover MB, Sivakumaran S, Donoghue J, Puryear CB. The role of sleep in Alzheimer's disease: a mini review. Front Neurosci. 2025;19:1428733. doi: 10.3389/fnins.2025.1428733
2. Matsumoto S, Tsunematsu T. Association between sleep, Alzheimer's, and Parkinson's disease. Biology. 2021;10(11):1127. doi: 10.3390/biology10111127
3. Jessen NA, Munk AS, Lundgaard I, Nedergaard M. The glymphatic system: a beginner's guide. Neurochem Res. 2015;40(12):2583-99. doi: 10.1007/s11064-015-1581-6
4. Morrone CD, Raghuraman R, Hussaini SA, Yu WH. Proteostasis failure exacerbates neuronal circuit dysfunction and sleep impairments in Alzheimer's disease. Mol Neurodegener. 2023;18(1):27. doi: 10.1186/s13024-023-00617-4
5. Tekieh T, Robinson PA, Postnova S. Cortical waste clearance in normal and restricted sleep with potential runaway tau buildup in Alzheimer's disease. Sci Rep. 2022;12(1):13740. doi: 10.1038/s41598-022-15109-6
6. Dijk DJ. Regulation and functional correlates of slow wave sleep. J Clin Sleep Med. 2009;5(2 Suppl):S6-15.
7. Roth T, Benca RM, Erman M. An introduction to the clinical correlates of disrupted slow-wave sleep. J Clin Psychiatry. 2010;71(4):e09. doi: 10.4088/JCP.9007tx1cc
8. Corbali O, Levey AI. Glymphatic system in neurological disorders and implications for brain health. Front Neurol. 2025;16:1543725. doi: 10.3389/fneur.2025.1543725
9. Hu Y, Xia X, Li H, Xie Y, Tian X, Li Y, et al. The association between sleep quality and cognitive impairment among a multi-ethnic population of middle-aged and older adults in Western China: a multi-center cross-sectional study. Front Public Health. 2025;13:1500027. doi: 10.3389/fpubh.2025.1500027
10. Yin C, Zhang M, Cheng L, Ding L, Lv Q, Huang Z, et al. Melatonin modulates TLR4/MyD88/NF-κB signaling pathway to ameliorate cognitive impairment in sleep-deprived rats. Front Pharmacol. 2024;15:1430599. doi: 10.3389/fphar.2024.1430599
11. Chachaj A, Gąsiorowski K, Szuba A, Sieradzki A, Leszek J. The lymphatic system in the brain clearance mechanisms - new therapeutic perspectives for Alzheimer's disease. Curr Neuropharmacol. 2023;21(2):380-91. doi: 10.2174/1570159x20666220411091332
12. Ben-Nejma IR, Keliris AJ, Vanreusel V, Ponsaerts P, Van der Linden A, Keliris GA. Altered dynamics of glymphatic flow in a mature-onset Tet-off APP mouse model of amyloidosis. Alzheimers Res Ther. 2023;15(1):23. doi: 10.1186/s13195-023-01175-z
13. Xin W, Pan Y, Wei W, Tatenhorst L, Graf I, Popa-Wagner A, et al. Preconditioned extracellular vesicles from hypoxic microglia reduce poststroke AQP4 depolarization, disturbed cerebrospinal fluid flow, astrogliosis, and neuroinflammation. Theranostics. 2023;13(12):4197-216. doi: 10.7150/

thno.84059
14. Formolo DA, Yu J, Lin K, Tsang HWH, Ou H, Kranz GS, et al. Leveraging the glymphatic and meningeal lymphatic systems as therapeutic strategies in Alzheimer's disease: an updated overview of nonpharmacological therapies. Mol Neurodegener. 2023;18(1):26. doi: 10.1186/s13024-023-00618-3
15. Kylkilahti TM, Berends E, Ramos M, Shanbhag NC, Töger J, Markenroth Bloch K, et al. Achieving brain clearance and preventing neurodegenerative diseases-a glymphatic perspective. J Cereb Blood Flow Metab. 2021;41(9):2137-49. doi: 10.1177/0271678x20982388
16. Järvelä M, Kananen J, Korhonen V, Huotari N, Ansakorpi H, Kiviniemi V. Increased very low frequency pulsations and decreased cardiorespiratory pulsations suggest altered brain clearance in narcolepsy. Commun Med (Lond). 2022;2:122. doi: 10.1038/s43856-022-00187-4
17. Zou W, Pu T, Feng W, Lu M, Zheng Y, Du R, et al. Blocking meningeal lymphatic drainage aggravates Parkinson's disease-like pathology in mice overexpressing mutated α-synuclein. Transl Neurodegener. 2019;8:7. doi: 10.1186/s40035-019-0147-y
18. Li H, Yao Q, Huang X, Yang X, Yu C. The role and mechanism of Aβ clearance dysfunction in the glymphatic system in Alzheimer's disease comorbidity. Front Neurol. 2024;15:1474439. doi: 10.3389/fneur.2024.1474439
19. Barmaki H, Nourazarian A, Khaki-Khatibi F. Proteostasis and neurodegeneration: a closer look at autophagy in Alzheimer's disease. Front Aging Neurosci. 2023;15:1281338. doi: 10.3389/fnagi.2023.1281338
20. Hipp MS, Park SH, Hartl FU. Proteostasis impairment in protein-misfolding and-aggregation diseases. Trends Cell Biol. 2014;24(9):506-14. doi: 10.1016/j.tcb.2014.05.003
21. Naidoo N. Sleep loss and the unfolded protein response. In: Pack AI, Li QY, eds. Sleep and its Disorders: Translational Medicine. Dordrecht: Springer; 2022. p. 127-47. doi: 10.1007/978-94-024-2168-2_7
22. Ortiz-Vega N, Lobato AG, Canic T, Zhu Y, Lazopulo S, Syed S, et al. Regulation of proteostasis by sleep through autophagy in *Drosophila* models of Alzheimer's disease. Life Sci Alliance. 2024;7(11):e202402681. doi: 10.26508/lsa.202402681
23. Bai Y, Yuan M, Mi H, Zhang F, Liu X, Lu C, et al. Hypothermia reduces glymphatic transportation in traumatic edematous brain assessed by intrathecal dynamic contrast-enhanced MRI. Front Neurol. 2022;13:957055. doi: 10.3389/fneur.2022.957055
24. Song AK, Hett K, Eisma JJ, McKnight CD, Elenberger J, Stark AJ, et al. Parasagittal dural space hypertrophy and amyloid-β deposition in Alzheimer's disease. Brain Commun. 2023;5(3):fcad128. doi: 10.1093/braincomms/fcad128
25. Hipp MS, Kasturi P, Hartl FU. The proteostasis network and its decline in ageing. Nat Rev Mol Cell Biol. 2019;20(7):421-35. doi: 10.1038/s41580-019-0101-y
26. Höhn A, Tramutola A, Cascella R. Proteostasis failure in neurodegenerative diseases: focus on oxidative stress. Oxid Med Cell Longev. 2020;2020:5497046. doi: 10.1155/2020/5497046
27. Zou K, Deng Q, Zhang H, Huang C. Glymphatic system: a gateway for neuroinflammation. Neural Regen Res. 2024;19(12):2661-72. doi: 10.4103/1673-5374.391312
28. Carpi M, Mercuri NB, Liguori C. Orexin receptor antagonists for the prevention and treatment of Alzheimer's disease and associated sleep disorders. Drugs. 2024;84(11):1365-78. doi: 10.1007/s40265-024-02096-3
29. Li Y, Wang L, Zhong J, Xu H, Han Y, Zuo C, et al. Impaired glymphatic function as a biomarker for subjective cognitive decline: an exploratory dual cohort study. Alzheimers Dement. 2024;20(9):6542-55. doi: 10.1002/alz.14149
30. Xu Z, Xiao N, Chen Y, Huang H, Marshall C, Gao J, et al. Deletion of aquaporin-4 in APP/PS1 mice exacerbates brain Aβ accumulation and memory deficits. Mol Neurodegener. 2015;10:58. doi: 10.1186/s13024-015-0056-1
31. Scott-Massey A, Boag MK, Magnier A, Bispo D, Khoo TK, Pountney DL. Glymphatic system dysfunction and sleep disturbance may contribute to the pathogenesis and progression of Parkinson's disease. Int J Mol Sci. 2022;23(21):12928. doi: 10.3390/ijms232112928
32. Li Y, Zhang T, Wang C, Geng L, Liu T, Lu T, et al. The impact of sleep disorders on glymphatic function in Parkinson's disease using diffusion tensor MRI. Acad Radiol. 2025;32(4):2209-19. doi: 10.1016/j.acra.2024.11.030
33. Cui H, Wang W, Zheng X, Xia D, Liu H, Qin C, et al. Decreased AQP4 expression aggravates α-synuclein pathology in Parkinson's disease mice, possibly via impaired glymphatic clearance. J Mol Neurosci. 2021;71(12):2500-13. doi: 10.1007/s12031-021-01836-4
34. Duan W, Zhou Y, Liu H. The glymphatic system in Huntington's disease. J Huntingtons Dis. 2025;14(3):279-90. doi: 10.1177/18796397251331436
35. Navarrete M, Osorio-Forero A, Gómez A, Henao D, Segura-Quijano FE, Le Van Quyen M, et al. Response of sleep slow oscillations to acoustic stimulation is evidenced by distinctive synchronization processes. Sleep. 2023;46(6):zsad110. doi: 10.1093/sleep/zsad110
36. Kong L, Jin W, Jiang Y, Yan F, Liu J, Leuthardt EC, et al. Transcranial vibration stimulation at 40 Hz induced neural activity and promoted the coupling of global brain activity and cerebrospinal fluid flow. Neuroimage. 2025;308:121074. doi: 10.1016/j.neuroimage.2025.121074
37. Bignold JJ, Mercer JD, Antic NA, McEvoy RD, Catcheside PG. Accurate position monitoring and improved supine-dependent obstructive sleep apnea with a new position recording and supine avoidance device. J Clin Sleep Med. 2011;7(4):376-83. doi: 10.5664/jcsm.1194
38. Lee H, Xie L, Yu M, Kang H, Feng T, Deane R, et al. The effect of body posture on brain glymphatic transport. J Neurosci. 2015;35(31):11034-44. doi: 10.1523/jneurosci.1625-15.2015
39. Kato D, Kameda H, Kinota N, Fujii T, Xiawei B, Simi Z, et al. Loss of aquaporin-4 impairs cerebrospinal fluid solute clearance through cerebrospinal fluid drainage pathways. Sci Rep. 2024;14(1):27982. doi: 10.1038/s41598-024-79147-y
40. Sun H, Cao Q, He X, Du X, Jiang X, Wu T, et al. Melatonin mitigates sleep restriction-induced cognitive and glymphatic dysfunction via aquaporin-4 polarization. Mol Neurobiol. 2025;62(9):11443-65. doi: 10.1007/s12035-025-04992-5
41. Mestre H, Tithof J, Du T, Song W, Peng W, Sweeney AM, et al. Flow of cerebrospinal fluid is driven by arterial pulsations and is reduced in hypertension. Nat Commun. 2018;9(1):4878. doi: 10.1038/s41467-018-07318-3
42. Andica C, Kamagata K, Takabayashi K, Kikuta J, Kaga H, Someya Y, et al. Neuroimaging findings related to glymphatic system alterations in older adults with metabolic syndrome. Neurobiol Dis. 2023;177:105990. doi: 10.1016/j.nbd.2023.105990
43. von Holstein-Rathlou S, Petersen NC, Nedergaard M. Voluntary running enhances glymphatic influx in awake behaving, young mice. Neurosci Lett. 2018;662:253-8. doi: 10.1016/j.neulet.2017.10.035
44. Kang KM, Park C, Byun MS, Yi D, Nam H, Ryu J, et al. APOE4 modulates the association between DTI-ALPS index and Alzheimer's pathologies. Alzheimers Dement. 2025;21(10):e70837. doi: 10.1002/alz.70837