



Review Article

THE GLYMPHATIC SYSTEM AND BRAIN HEALTH: A NARRATIVE REVIEW OF SLEEP, HYDRATION, AND LIFESTYLE FACTORS

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ABSTRACT

Background

The glymphatic system is a proposed brain-wide pathway involved in cerebrospinal fluid movement and the clearance of metabolic waste from the central nervous system. Increasing evidence suggests that sleep, particularly slow-wave sleep, may influence cerebrospinal fluid dynamics and processes involved in cerebral waste clearance. These mechanisms may have important implications for maintaining brain homeostasis and neurological health.

Methods

A structured narrative review was conducted to synthesize evidence on glymphatic physiology and its relationships with sleep, metabolic waste clearance, hydration, aging, lifestyle factors, and brain health. Relevant literature was identified from biomedical and scientific databases using terms related to the glymphatic system, cerebrospinal fluid, sleep, slow-wave sleep, aquaporin-4, amyloid-beta, aging, and neurodegenerative disease. Peer-reviewed experimental studies, human investigations, systematic reviews, and authoritative reviews were considered. Findings were synthesized narratively without quantitative statistical pooling.

Results

Available evidence indicates that glymphatic pathways may contribute to the movement of cerebrospinal and interstitial fluids and the clearance of extracellular solutes, including amyloid-beta. Experimental and emerging human studies demonstrate associations between sleep and coordinated changes in neural activity, vascular dynamics, and cerebrospinal fluid movement. Aging, vascular alterations, sleep disruption, and changes in aquaporin-4 organization have also been associated with altered glymphatic function. However, evidence directly establishing glymphatic dysfunction as a cause of neurological disease remains limited, and the specific effects of hydration and lifestyle interventions on glymphatic clearance require further investigation.

Conclusion

The glymphatic system represents an emerging mechanism potentially involved in maintaining cerebral fluid homeostasis and metabolic waste clearance. Sleep may support these physiological processes, while aging, vascular health, and lifestyle factors may influence their regulation. Further well-designed human studies using standardized methods are needed to clarify the clinical relevance of glymphatic function and its potential implications for brain-health promotion, nursing, medical practice, and public health.

(Key Word:- Glymphatic system; Cerebrospinal fluid; Metabolic waste clearance; Sleep; Slow-wave sleep; Aquaporin-4; Brain health; Aging; Neurodegenerative disease.)

INTRODUCTION

The human brain has exceptionally high metabolic demands and requires continuous energy production to sustain neuronal signalling, synaptic activity, and cellular homeostasis. These processes generate a variety of

metabolic by-products, including proteins, peptides, ions, and other cellular waste that must be efficiently transported and eliminated. Maintaining an appropriate extracellular environment is essential for normal neuronal function, as persistent accumulation of unwanted substances may disturb cellular signalling and contribute to neural stress. Unlike most peripheral tissues, the central nervous system

has specialized anatomical and physiological mechanisms for regulating fluid movement and maintaining its internal environment.

The glymphatic system was proposed as a brain-wide pathway involved in the movement of cerebrospinal fluid (CSF) and interstitial fluid through perivascular spaces. In this model, CSF enters the brain along peri-arterial pathways and exchanges with interstitial fluid, facilitating the transport of extracellular solutes toward drainage routes associated with peri-venous spaces and lymphatic pathways. The term “glymphatic” reflects the proposed involvement of glial cells and the functional resemblance of this pathway to the peripheral lymphatic system. Astrocytic aquaporin-4 (AQP4) water channels have also been implicated in the regulation of fluid movement within this system. [1,2]

Interest in the glymphatic system has increased because the efficient clearance of metabolic waste may be relevant to long-term brain health. Experimental research has examined its role in the transport of substances such as amyloid-beta and other extracellular solutes. [1,3] Glymphatic transport has subsequently been investigated in relation to aging, vascular function, sleep, and neurological disorders. Although the precise mechanisms and clinical significance of glymphatic clearance in humans remain under investigation, these findings have provided a framework for understanding how brain fluid dynamics may contribute to the maintenance of neural homeostasis.

Sleep has emerged as an important factor in this area of research. Experimental studies have reported changes in CSF movement, extracellular-space dynamics, and solute transport during sleep, particularly during periods associated with slow-wave activity. [4,5] These observations have led to the hypothesis that sleep may provide a physiological state that supports processes involved in brain maintenance and metabolic waste clearance. Disturbances in sleep may therefore be relevant to the regulation of these processes, although the direction and strength of the relationship between sleep, glymphatic function, and neurological disease require further investigation.

The relationship between glymphatic function and brain health is particularly relevant because effective fluid and solute clearance may help preserve the brain's extracellular environment. Factors such as aging, vascular changes, sleep patterns, hydration status, and lifestyle have been proposed as potential modifiers of glymphatic activity. Understanding these interactions may provide broader insight into mechanisms involved in maintaining cognitive and neurological health and may help identify areas relevant to preventive health and supportive clinical care.

The objective of this narrative review is to summarize current evidence concerning the glymphatic system and

its relationship with sleep, metabolic waste clearance, hydration, aging, lifestyle, and neurological health, with consideration of potential implications for nursing, medical practice, and public health.

METHODS

This narrative review was developed through a structured examination of published scientific literature concerning glymphatic physiology and its relationship with sleep, metabolic waste clearance, and brain health. Relevant literature was identified from biomedical and scientific databases using combinations of terms including “glymphatic system,” “glymphatic clearance,” “cerebrospinal fluid,” “sleep,” “slow-wave sleep,” “aquaporin-4,” “brain waste clearance,” “amyloid-beta,” “aging,” and “neurodegenerative disease.”

Priority was given to peer-reviewed experimental studies, human investigations, systematic reviews, and authoritative scientific reviews. Publications addressing the physiological basis of glymphatic transport and its potential relationship with neurological health were considered. Because the purpose of the review was narrative synthesis rather than quantitative meta-analysis, statistical pooling of study findings was not undertaken.

The available evidence was critically interpreted with particular attention to the distinction between established physiological observations, experimental findings, and emerging hypotheses. Findings from animal and human studies were considered in their respective contexts, and claims for which human clinical evidence remains limited were presented cautiously. Methodological and conceptual limitations within the existing literature were also considered, including differences in study models, methods used to assess glymphatic activity, and uncertainty regarding the extent to which experimental findings can be directly translated to human brain physiology. The review therefore aims to provide a balanced synthesis of current knowledge while identifying areas requiring further investigation.

RESULTS

3.1 Glymphatic System and Cerebral Waste Clearance

The glymphatic system describes a proposed pathway for the movement of CSF and interstitial fluid through the brain. In the model initially described by Iliff et al., CSF enters the brain along periarial spaces and exchanges with interstitial fluid before waste-containing fluid moves toward perivenous pathways. Astrocytes and their AQP4 water channels are thought to facilitate aspects of this fluid exchange. [1]

Nedergaard and colleagues subsequently proposed that this pathway represents an important component of waste clearance in the central nervous system. [2] Experimental

studies have demonstrated that the pathway can contribute to the transport of soluble molecules through brain tissue.

The lymphatic system associated with the meninges also provides an important route for drainage from the central nervous system. Studies demonstrating meningeal lymphatic vessels have expanded understanding of how CSF and immune-related substances may ultimately reach peripheral lymphatic and systemic circulation. [6,7]

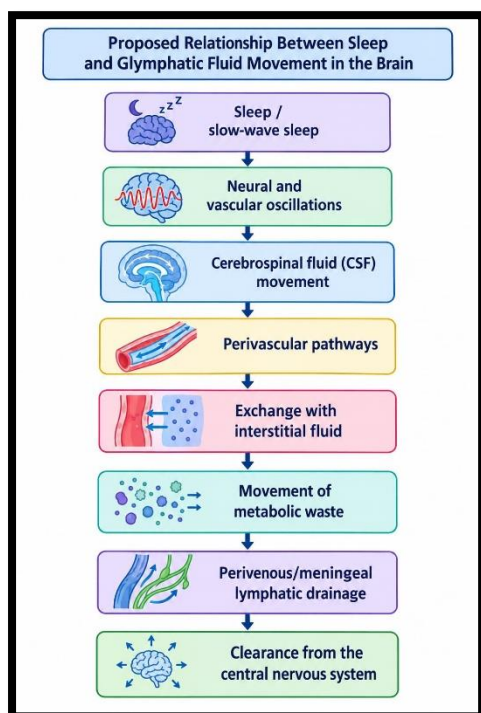
3.2 Sleep and Glymphatic Activity

Sleep has emerged as one of the most extensively investigated physiological factors associated with glymphatic function. Xie et al. reported that sleep was associated with increased interstitial-space volume and enhanced clearance of certain metabolites in experimental animals. [4]

More recent research has examined relationships between slow-wave activity, CSF dynamics, and vascular pulsatility. Fultz et al. demonstrated coordinated changes in neural activity, CSF flow, and hemodynamic signals during human non-rapid eye movement sleep, providing evidence for a close relationship between sleep physiology and CSF dynamics. [5]

These findings suggest that sleep may provide a physiological environment favorable to brain-fluid movement and waste transport. However, the precise mechanisms and their clinical significance in humans remain under investigation.

Figure 1. Proposed relationship between sleep and glymphatic fluid movement in the brain.



3.3 Metabolic Waste and Neurodegenerative Disease

Amyloid-beta and tau proteins are among the substances of greatest interest in research on brain clearance. Impaired clearance of amyloid-beta has been implicated in the pathophysiology of Alzheimer disease, while abnormal tau accumulation is strongly associated with neurodegeneration. [8,9]

Animal studies have suggested that glymphatic transport contributes to amyloid-beta clearance. [3] Alterations in AQP4 localization and glymphatic function have also been investigated in aging and neurodegenerative disease. [10]

Nevertheless, it is important to distinguish association from causation. Although glymphatic dysfunction may contribute to pathological processes, current evidence does not establish that impaired glymphatic clearance is a single or sufficient cause of Alzheimer disease, Parkinson disease, or other neurodegenerative conditions.

3.4 Sleep Deprivation and Brain Health

Chronic insufficient sleep is associated with adverse cognitive, metabolic, cardiovascular, and psychological outcomes. Experimental evidence suggests that sleep deprivation can influence brain-fluid dynamics and the clearance of metabolic substances. [4,11]

A growing body of human research also indicates relationships between sleep quality and biomarkers associated with neurodegeneration. For example, sleep disruption has been associated with alterations in amyloid-beta and tau metabolism. [11,12]

These observations reinforce the importance of adequate and regular sleep as a component of overall brain-health promotion. However, the concept that a specific number of hours of sleep directly "detoxifies" the brain through the glymphatic system should be presented cautiously because human glymphatic physiology is not yet fully understood.

3.5 Hydration and Cerebrospinal-Fluid Dynamics

Water is essential for normal cellular function and constitutes a major component of brain tissue and body fluids. Dehydration may affect attention, alertness, and cognitive performance, particularly when substantial. [13]

Because the glymphatic system depends on fluid movement involving CSF and interstitial fluid, fluid balance is biologically relevant to its function. Nevertheless, direct clinical evidence demonstrating that drinking additional water specifically increases glymphatic clearance in healthy adults is currently insufficient.

Therefore, maintaining adequate hydration should be considered an established general health recommendation rather than a proven method of directly enhancing glymphatic clearance.

3.6 Aging and Glymphatic Function

Aging is associated with structural and physiological changes in the brain, including alterations in vascular function, sleep architecture, and CSF dynamics. Research has suggested that glymphatic transport may decline with age and that changes in AQP4 distribution may contribute to impaired clearance. [10,14]

Age-related reduction in sleep quality may provide an additional mechanism through which brain clearance processes are affected. Because aging is also the major risk factor for many neurodegenerative disorders, understanding these interactions may have important implications for healthy aging.

3.7 Lifestyle Factors and Brain Health

Lifestyle factors influence neurological health through multiple pathways, including vascular, metabolic, inflammatory, and sleep-related mechanisms. Regular physical activity has been associated with beneficial effects on cognitive health and may influence mechanisms relevant to CSF circulation and brain waste clearance. [15]

Similarly, management of cardiovascular risk factors, balanced nutrition, adequate sleep, stress management, and avoidance of harmful substances are established components of comprehensive brain-health promotion.

Evidence specifically demonstrating that each of these interventions directly enhances glymphatic function in humans remains limited. Consequently, lifestyle recommendations should primarily be based on their established benefits for overall neurological and cardiovascular health

Table 1. Factors potentially influencing glymphatic function and implications for brain health

S. N o.	Factor	Potential relationship with glymphatic function	Current evidence	Relevance to brain health
1	Adequate sleep	May support CSF movement and metabolic waste clearance	Experimental evidence is strong; human evidence is emerging	Supports cognitive and neurological health
2	Slow-wave sleep	Associated with coordinated neural, vascular, and CSF oscillations	Increasing evidence from human studies	May contribute to physiological brain

S. N o.	Factor	Potential relationship with glymphatic function	Current evidence	Relevance to brain health
				maintenance
3	Sleep deprivation	May impair metabolic waste clearance and alter CSF dynamics	Experimental and observational evidence	Associated with impaired cognition and adverse health outcomes
4	Aging	May reduce efficiency of perivascular clearance pathways	Experimental and human evidence	May contribute to vulnerability to neurological disorders
5	Physical activity	May influence vascular and fluid-related mechanisms	Direct glymphatic evidence remains limited	Established benefits for cardiovascular and cognitive health
6	Hydration	Maintains normal body-fluid and CSF homeostasis	General physiological evidence; direct glymphatic evidence is limited	Important for normal cognitive and physical function
7	Cardiovascular health	Vascular pulsatility may influence CSF/interstitial-fluid movement	Biologically plausible; research ongoing	Important for long-term cerebrovascular and brain health
8	Stress	May indirectly affect glymphatic function through sleep and physiological changes	Direct evidence is limited	Chronic stress may adversely affect sleep and overall health

Source: Compiled from the literature reviewed in this article. [1,4,5,10,14,15]

3.8 Potential Implications for Nursing and Public Health

The emerging glymphatic-system literature has relevance to nursing and public health because sleep, hydration, physical activity, stress management, and healthy aging are modifiable factors that can be addressed through health education and preventive care.

Nurses are well positioned to assess sleep patterns, identify sleep-related problems, provide sleep-hygiene education, encourage appropriate physical activity, and promote healthy lifestyle behaviours. Public-health professionals can incorporate sleep health and brain-health promotion into community education and healthy-aging programs.

However, health professionals should avoid presenting the glymphatic system as a proven “brain detox” mechanism or promising that individual lifestyle interventions can prevent neurodegenerative disease. Communication should reflect the current level of scientific evidence.

DISCUSSION

The glymphatic system has emerged as an important framework for understanding how fluid movement may contribute to metabolic waste clearance in the central nervous system. Experimental evidence supports the existence of perivascular pathways involved in CSF-interstitial fluid exchange, while research in humans has demonstrated relationships between sleep and CSF dynamics. [1,4,5]

One of the most important developments has been the recognition that sleep is associated with coordinated physiological changes within the brain. During non-rapid eye movement sleep, neural activity, vascular dynamics, and CSF movement appear to interact. [5] This provides a plausible physiological basis for the hypothesis that sleep contributes to brain maintenance.

The potential relationship between glymphatic dysfunction and neurodegenerative disease is particularly significant. Alzheimer disease is characterized by accumulation of amyloid-beta and abnormal tau pathology, and research suggests that altered clearance mechanisms may contribute to disease progression. [8,9] However, neurodegenerative disease is multifactorial, and glymphatic dysfunction should not be considered an established single cause.

The role of AQP4 is also important. Experimental evidence indicates that AQP4 polarization around cerebral blood vessels is associated with glymphatic transport. [10] Changes in AQP4 organization during aging and disease may therefore represent a possible mechanism linking vascular, glial, and clearance abnormalities.

From a clinical perspective, the most practical implication is not the promotion of a specific “detoxification” protocol but reinforcement of established brain-health behaviors. Adequate sleep, physical activity, appropriate hydration, balanced nutrition, and management of cardiovascular risk factors have broad health benefits. These measures can reasonably be recommended while research continues to determine their specific effects on glymphatic physiology.

For nursing practice, the glymphatic concept can provide an additional scientific framework for explaining why sleep and healthy lifestyle behaviors are important. Sleep assessment and education should be incorporated into holistic nursing care, particularly among older adults and individuals at risk of neurological or cardiometabolic disease.

For public health, increasing awareness of sleep health represents a potentially valuable preventive strategy. Community interventions addressing sleep duration, sleep quality, physical activity, obesity, hypertension, diabetes, and cardiovascular health may have benefits extending beyond glymphatic physiology to overall neurological resilience.

LIMITATIONS

This review has several limitations. First, it is a narrative rather than systematic review and therefore does not provide quantitative synthesis of the available evidence. Second, a substantial proportion of mechanistic evidence concerning glymphatic transport originates from animal and experimental studies. Third, methods used to assess glymphatic function in humans vary considerably, and there is currently no universally accepted clinical measure of glymphatic activity.

Furthermore, the relationship between glymphatic function and neurodegenerative disease remains an active area of research. Some findings are associative, and causal relationships cannot yet be established confidently. Future longitudinal human studies using standardized biomarkers and imaging techniques are required.

RECOMMENDATIONS FOR FUTURE RESEARCH

Future research should focus on improving the understanding of glymphatic function in humans through well-designed and standardized studies. Longitudinal research is needed to clarify how sleep, aging, vascular health, hydration, physical activity, and other lifestyle factors are related to changes in glymphatic activity over time. Further human studies should use reliable imaging techniques and validated biomarkers to improve the assessment of glymphatic-related processes. Interventional studies are also needed to determine whether improving sleep quality, physical activity, cardiovascular health, or

other modifiable lifestyle factors produces measurable changes in glymphatic function. Research should additionally examine the clinical relevance of glymphatic alterations in neurological and neurodegenerative conditions while clearly distinguishing established associations from causal relationships. Multidisciplinary collaboration among neuroscience, nursing, medicine, public health, and allied health researchers may further support the translation of emerging evidence into clinically appropriate brain-health strategies.

CONCLUSION

The glymphatic system represents an emerging area of neuroscience that has expanded understanding of how CSF and interstitial fluid may contribute to cerebral waste clearance. Evidence indicates that sleep is closely associated with brain-fluid dynamics and may provide a physiological state favourable to metabolic waste transport. Aging, vascular dysfunction, sleep disruption, and neurological disease may influence these processes.

Although the concept of the glymphatic system is scientifically promising, evidence should be communicated cautiously. At present, there is insufficient clinical evidence to describe the system simply as a “brain detox system” or to claim that specific lifestyle interventions directly prevent neurodegenerative disease by increasing glymphatic clearance.

Nevertheless, adequate sleep, regular physical activity, appropriate hydration, healthy nutrition, stress management, and control of cardiovascular risk factors remain important components of comprehensive brain-health promotion. Nurses, medical professionals, and public-health practitioners can play an important role in translating emerging neuroscience into practical, evidence-based health education.

DECLARATIONS

Ethics approval and consent to participate

Not applicable. This article is a narrative review based on previously published literature and did not involve human participants, animal subjects, or the collection of primary data.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable. This article is based on information available in the published literature cited in the manuscript.

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Author Contribution

The author was responsible for the conception of the review, literature identification, synthesis and interpretation of the available evidence, manuscript preparation, critical revision, and final approval of the manuscript.

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