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Cerebral small vessel disease: The impact of glymphopathy and sleep disorders

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Abstract

The glymphatic system, a vital brain perivascular network for waste clearance, hinges on the functionality of the aquaporin 4 (AQP4) water channel. Alarmingly, AQP4 single nucleotide polymorphisms (SNPs) are linked to impaired glymphatic clearance, or glymphopathy, which contributes to sleep disturbances and various age-related neurodegenerative diseases. Despite the critical role of glymphopathy and sleep disturbances in cerebral small vessel disease (CSVD) – a silent precursor to age-related neurodegenerative disorders – their interplay remains underexplored. CSVD is a major cause of stroke and dementia, yet its pathogenesis is not fully understood. Emerging evidence implicates glymphopathy and sleep disorders as pivotal factors in

age-related CSVD, exacerbating the condition by hindering waste removal and compromising blood-brain barrier (BBB) integrity. Advanced imaging techniques promise to enhance diagnosis and monitoring, while lifestyle modifications and personalised medicine present promising treatment avenues. This narrative review underscores the need for a multidisciplinary approach to understanding glymphopathy and sleep disorders in CSVD. By exploring their roles, emphasising the necessity for longitudinal studies, and discussing potential therapeutic interventions, this paper aims to pave the way for new research and therapeutic directions in CSVD management. © The Author(s) 2025

Author keywords

aquaporin 4; Cerebral small vessel disease; glymphatic system; glymphopathy; sleep

Indexed keywords

MeSH

Aquaporin 4; Blood-Brain Barrier; Cerebral Small Vessel Diseases; Glymphatic System; Humans; Sleep Wake Disorders

EMTREE drug terms

aquaporin 4; aquaporin 4

EMTREE medical terms

blood brain barrier; cerebrovascular accident; controlled study; degenerative disease; dementia; diagnosis; etiology; glymphatic system; human; lifestyle modification; longitudinal study; major clinical study; pathogenesis; personalized medicine; review; single nucleotide polymorphism; sleep; sleep disorder; cerebrovascular disease; complication; genetics; metabolism; pathology; pathophysiology

Chemicals and CAS Registry Numbers

Unique identifiers assigned by the Chemical Abstracts Service (CAS) to ensure accurate identification and tracking of chemicals across scientific literature.

aquaporin 4

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Aquaporin 4

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