

## Objective

This systematic review aims to comprehensively investigate the involvement of the glymphatic system (GS) and its integral component, aquaporin 4, in the formation of cerebral edema, as well as explore emerging therapeutic approaches for ischemic stroke.

## Methods

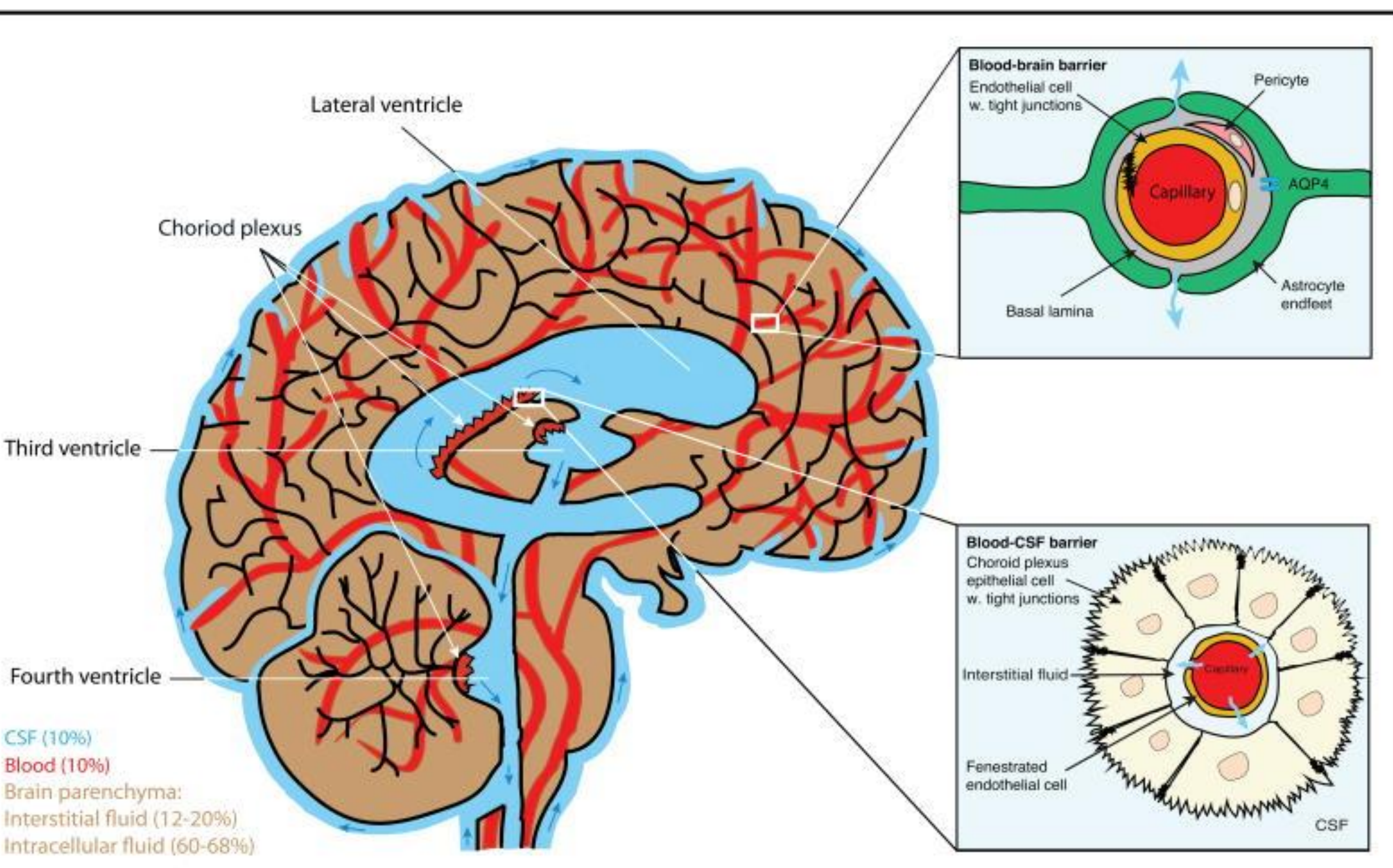
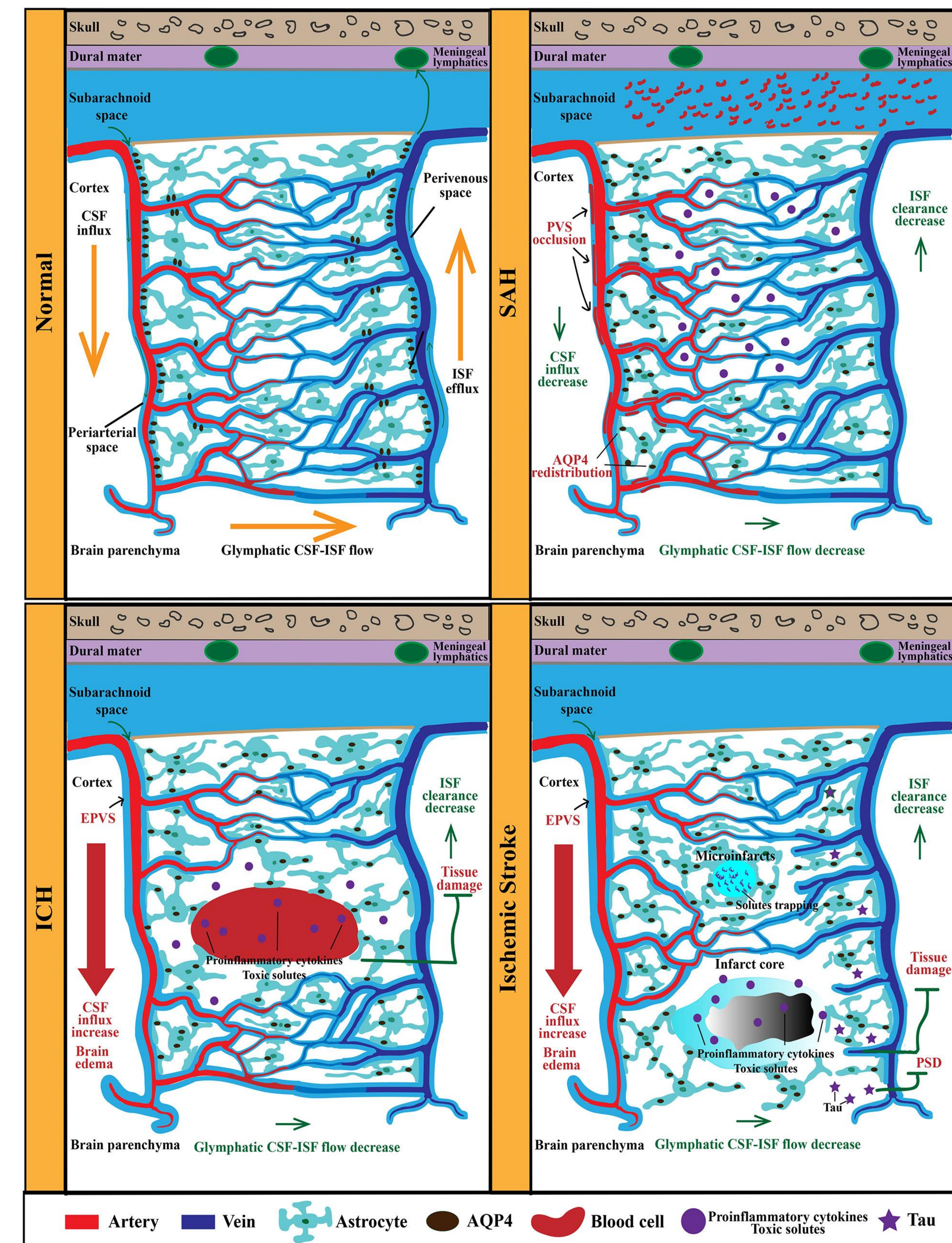
A comprehensive search was conducted in PubMed, PMC, and Cochrane Library databases, spanning the period from January 2015 to December 2022. The PRISMA flowchart guided the selection process, ultimately identifying five relevant studies for inclusion. Quality assessment tools were employed to address potential bias. Studies chosen have animal models utilized as both intervention and control groups to assess GS participation in cerebral edema formation and its responsiveness to therapeutic interventions.

## Result

The glymphatic system is compromised in the context of ischemic stroke. Findings from this study reveal that in the early stages of stroke, there is an increased cerebrospinal fluid (CSF) inflow within the GS, coupled with a decreased outflow, consequently contributing to cerebral edema. This disrupted GS flow results in the accumulation of detrimental metabolites and deposits, which further exacerbate post-stroke complications including dementia. Hence, restoring proper GS function holds pivotal importance in ischemic stroke management. Notably, aquaporin 4, a critical component of the GS, plays a dual role in this context. Changes in aquaporin expression and mislocalization during ischemic stroke contribute to cerebral edema by impairing solute and water flow within the GS. Conversely, aquaporin 4 enhances flow along the venous aspect of the GS, mitigating cerebral edema. Both in vitro and in vivo investigations have highlighted therapeutic prospects through aquaporin 4 inhibition or deletion, coupled with GS restoration, effectively reducing cerebral edema. Selective aquaporin 4 inhibition emerges as a promising strategy, significantly curbing inflow and enhancing outflow within the GS, thereby attenuating edema following ischemic stroke and ultimately reducing morbidity.

## Conclusion

Ischemic stroke disrupts the integrity of aquaporin 4 channels, consequently impairing the glymphatic system and contributing to cerebral edema. Nonetheless, a deeper comprehension of the pathophysiology and innovative research into therapeutic interventions is imperative to unravel the complete role of the GS in ischemic stroke.



## References

- The role of glymphatic system in the cerebral edema formation after ischemic stroke <https://pubmed.ncbi.nlm.nih.gov/33676917/>  
The Glymphatic System: A Novel Therapeutic Target for Stroke Treatment <https://pubmed.ncbi.nlm.nih.gov/34305569/>