



## The role of the cerebellum in anoxic–ischemic brain damage and neurological clinical trials

Dear Editor,

I am writing to explore the highlights, pivotal role of the cerebellum in anoxic-ischemic brain damage and its implications for neurological clinical trials, offering insights for managing brain injuries. First, drowning remains a significant cause of neurological impairment in young children, leading to ABI. Recent studies employing voxel-based morphometry have elucidated profound gray and white matter changes in the ABI of pediatric patients, emphasizing the impact of vascular distribution on tissue loss (McMillan et al., 2024). These findings not only deepen our understanding of the pathophysiological mechanisms involved but also pave the way for targeted diagnostic and therapeutic interventions (Ishaque et al., 2016). In parallel, significant efforts have been made to address the narrow window of treatment for ischemic stroke. A recent study highlighted in your journal revealed promising results targeting the BEST1 channel, which plays a crucial role in mediating delayed excitotoxicity via extrasynaptic glutamate release. This breakthrough extends the therapeutic window to 72 hours postischemia, indicating that BEST1 is a potential therapeutic target with profound implications for stroke management (Xiong et al., 2023). Furthermore, the interplay of ionic imbalances and energy depletion in conditions such as ischemia, trauma, and epilepsy underscores the urgency of immediate interventions such as thrombolysis and rapid reperfusion in ischemic stroke. While these treatments are pivotal, translating experimental findings into clinical efficacy remains a challenge, prompting continued exploration of effective measures to mitigate long-term neurological sequelae (Cottrell et al., 2024). Importantly, integrating these insights calls for a multidisciplinary approach in clinical practice. Strategies to prevent complications such as hypoxia and hyperthermia have emerged as pivotal for improving overall outcomes for patients with neurological injuries (Mulla et al., 2024). Optimizing therapeutic interventions must consider not only acute management but also long-term neuroprotective strategies that mitigate secondary damage and enhance recovery (Dammavalam et al., 2024). Perinatal and neonatal care have improved survival rates for preterm infants, prompting a focus on enhancing neurological outcomes. Antenatal steroids and magnesium offer short-term benefits but have limited impact on long-term neurodevelopment (Molloy et al., 2024). Effective measures include preventing complications such as hypoxia and hyperthermia to improve long-term outcomes.

In conclusion, this study significantly contributes to our understanding of the role of the cerebellum in anoxic-ischemic brain damage and its implications for neurological clinical trials. Addressing the suggested areas for improvement could enhance the article's clarity and utility for its readers. I appreciate the opportunity to provide feedback and look forward to seeing how these enhancements might further advance the important work presented in the study.

<https://doi.org/10.1016/j.bas.2024.102865>

Received 4 July 2024; Accepted 10 July 2024

Available online 10 July 2024

2772-5294/© 2024 The Author(s). Published by Elsevier B.V. on behalf of EUROSPINE, the Spine Society of Europe, EANS, the European Association of Neurosurgical Societies. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### CRediT authorship contribution statement

Azhagu Madhavan Sivalingam: Writing – original draft, Writing – review & editing, Conceptualization, Supervision. Arjun Pandian: Formal analysis. All the authors gave final approval of the version to be submitted.

### Ethical approval

Not applicable.

### Funding sources

This study received no funding.

### Consent for publication

Not applicable.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgments

The corresponding author, Assistant Prof. Azhagu Madhavan Sivalingam, is thankful to all the authors for their collaborative efforts in writing this paper. This work is supported by the Natural Products & Nanobiotechnology Research Lab, Department of Community Medicine, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Thandalam, Chennai-600 105, Tamil Nadu, India.

### References

- Cottrell, J.E., Kass, I.S., Abramowicz, A.E., Hou, J.Y., Lei, B., 2024. 1 - brain metabolism, the pathophysiology of brain injury, and potential beneficial agents and techniques. In: Cottrell, J.E., Patel, P.M., Soriano, S.G. (Eds.), Cottrell & Patel's Neuroanesthesia, seventh ed. Elsevier, New Delhi, pp. 1–21.
- Dammavalam, V., Lin, S., Nessa, S., Daksla, N., Stefanowski, K., Costa, A., Bergese, S., 2024. Neuroprotection during thrombectomy for acute ischemic stroke: a review of future therapies. *Int. J. Mol. Sci.* 25 (2), 891.
- Ishaque, M., Manning, J.H., Woolsey, M.D., Franklin, C.G., Tullis, E.W., Fox, P.T., 2016. Lenticulostriate arterial distribution pathology may underlie pediatric anoxic brain injury in drowning. *Neuroimage: Clinical* 11, 167–172. <https://doi.org/10.1016/j.nicl.2016.01.019>.

- McMillan, K., Shaw, H., Hemesley, A., Zaman, W., Qazim, N., 2024. Neurological observations in infants, children and young people: part one. *Nurs. Child. Young People* 36 (1).
- Molloy, E.J., El-Dib, M., Soul, J., Juul, S., Gunn, A.J., Bender, M., et al., 2024. Neuroprotective therapies in the NICU in preterm infants: present and future (Neonatal Neurocritical Care Series). *Pediatr. Res.* 95 (5), 1224–1236. <https://doi.org/10.1038/s41390-023-02895-6>.
- Mulla, S., Gejji, J., Patel, K., 2024. Anesthetic considerations for patients with neurological disorders: a comprehensive review of current evidence. Paper Presented at the Obstetrics and Gynaecology Forum.
- Xiong, S., Xiao, H., Sun, M., Liu, Y., Gao, L., Xu, K., et al., 2023. Glutamate-releasing BEST1 channel is a new target for neuroprotection against ischemic stroke with wide time window. *Acta Pharm. Sin. B* 13 (7), 3008–3026. <https://doi.org/10.1016/j.apsb.2023.05.012>.

Azhagu Madhavan Sivalingam\*

*Natural Products & Nanobiotechnology Research Lab, Department of Community Medicine, Saveetha Medical College and Hospital, Saveetha*

*Institute of Medical and Technical Sciences (SIMATS), (Saveetha Deemed to be University), Thandalam, Chennai, 600 105, Tamil Nadu, India*

Arjun Pandian  
*Centre for Advanced Research, Institute of Biotechnology, Saveetha School of Engineering (SSE), Saveetha Institute of Medical and Technical Sciences (SIMATS), Thandalam, Chennai, 602105, Tamil Nadu, India*

\* Corresponding author.

E-mail addresses: [mathavan062@gmail.com](mailto:mathavan062@gmail.com), [azhugumadhavans.smc@saveetha.com](mailto:azhugumadhavans.smc@saveetha.com) (A.M. Sivalingam).

Handling Editor: Dr W Peul