Healthcare Innovations
How practice has changed

HERSTON HEALTH PRECINCT SYMPOSIUM 2021

DISC-0046

6 - 10 September 2021
Education Centre
RBWH

Evolution of Blood-Brain-Barrier disruption after Hypoxic-Ischemic injury in a neonatal piglet model.

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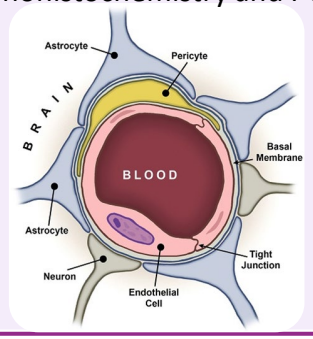
Background

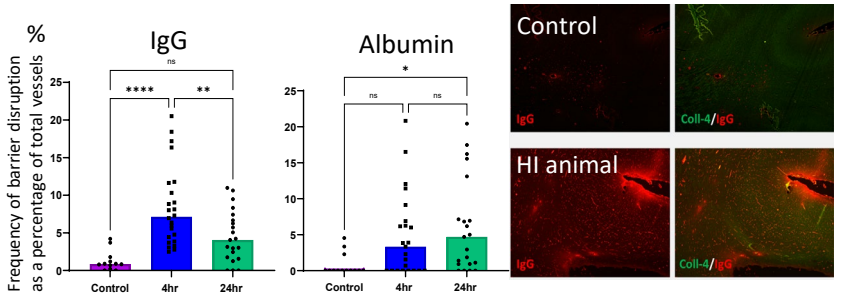
Hypoxic-ischemic (HI) insult (lack of oxygen and blood flow to the brain) around the time of birth leads to **hypoxic-ischemic encephalopathy (HIE)** a devastating neurological disorder in neonates. Which results in epilepsy, motor and cognitive impairments and cerebral palsy. **HI** injury evolves over time with a multitude of detrimental cascades being initiated, including **blood-brain barrier (BBB)** disruption.

The **BBB** is vital in ensuring the correct environment for brain function and protecting the brain from toxins. This study used newborn piglets to assess the evolution of BBB disruption after **HI**. Newborn piglets underwent a **HI** injury before being euthanized at different time points **(4&24hr)** we then sought to investigate **BBB** damage in these animals, using immunohistochemistry and PCR.

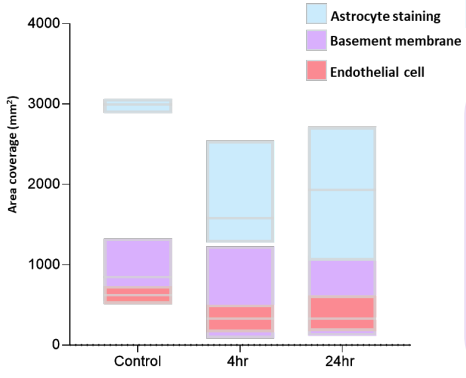


Results

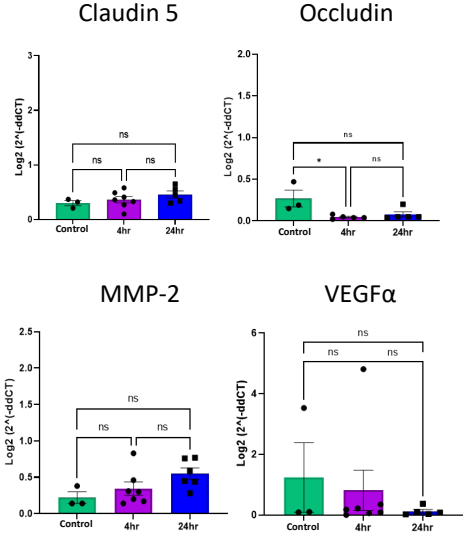
- BBB permeability is detrimentally decreased at both timepoints in the basal ganglia – seen as increased frequency of blood proteins (IgG & Albumin) infiltrating the barrier



- BBB component cells coverage is reduced at 4&24hrs compared to control
- Coverage alterations cause disruption to BBB integrity and signalling impacting functionality



- Important proteins at the tight junction on the barrier = No significantly altered gene expression
- Common Pathways induced post-HI that impact BBB components = No significantly altered gene expression



Conclusion

Temporal changes to **BBB** over time are not overt and not seen at the time points investigated.

BBB disruption is still apparent however the mechanisms need more investigation.

Understanding further how **HI** injury cascade evolves over time will allow targeted treatment design.

Griffith University Queensland, Australia · Menzies Health Institute Queensland · QIMR Berghofer Medical Research Institute The Future of Health · pathology queensland · QUT · The University of Queensland Australia Create Change · Herston Health Precinct · RBWH Foundation · Metro North Health · Queensland Government

Evolution of blood-brain-barrier disruption after hypoxic-ischemic injury in a neonatal piglet model.

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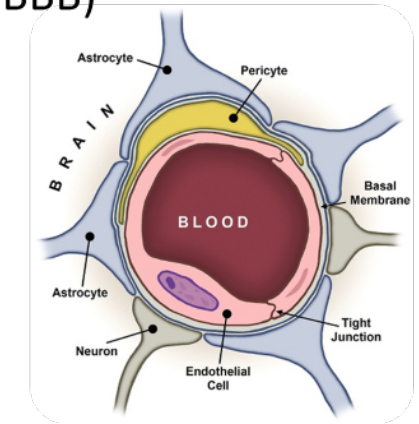
Background – brief methods

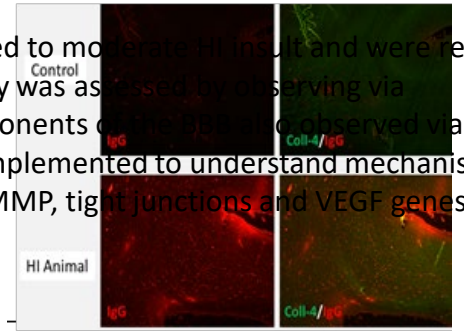
Newborn piglets (<24h old) were subjected to moderate HI insult and were recovered and euthanised at 4h or 24h. BBB permeability was assessed by observing via immunofluorescence (IF). Structural components of the BBB were observed via IF and were assessed for their localisation. PCR was implemented to understand mechanistic changes relating to BBB, looking at expression of MMP, tight junctions and VEGF genes across the two time-points.

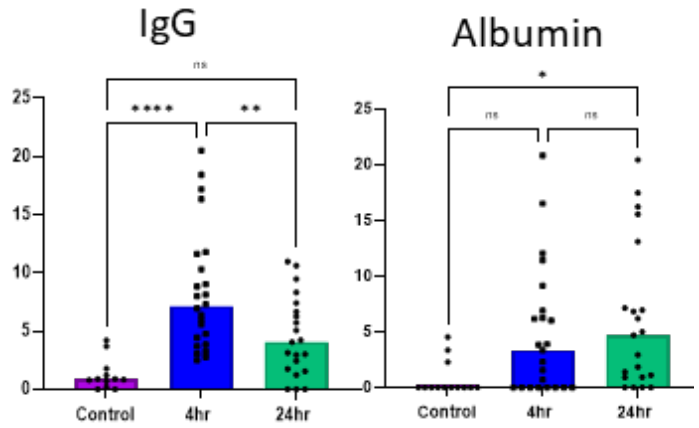
Blood-Brain-Barrier (BBB)



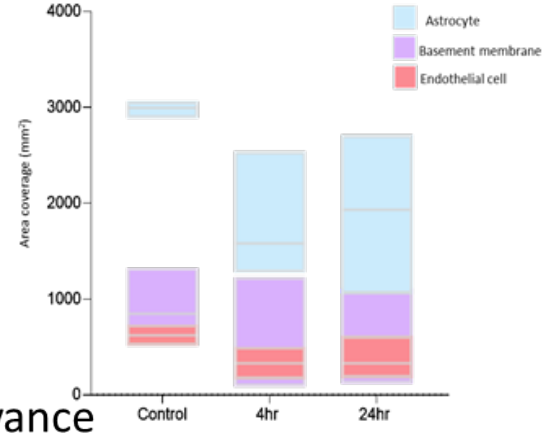
Results

- BBB permeability is detrimentally decreased at both timepoints – seen as increased frequency of blood proteins infiltrating the BBB

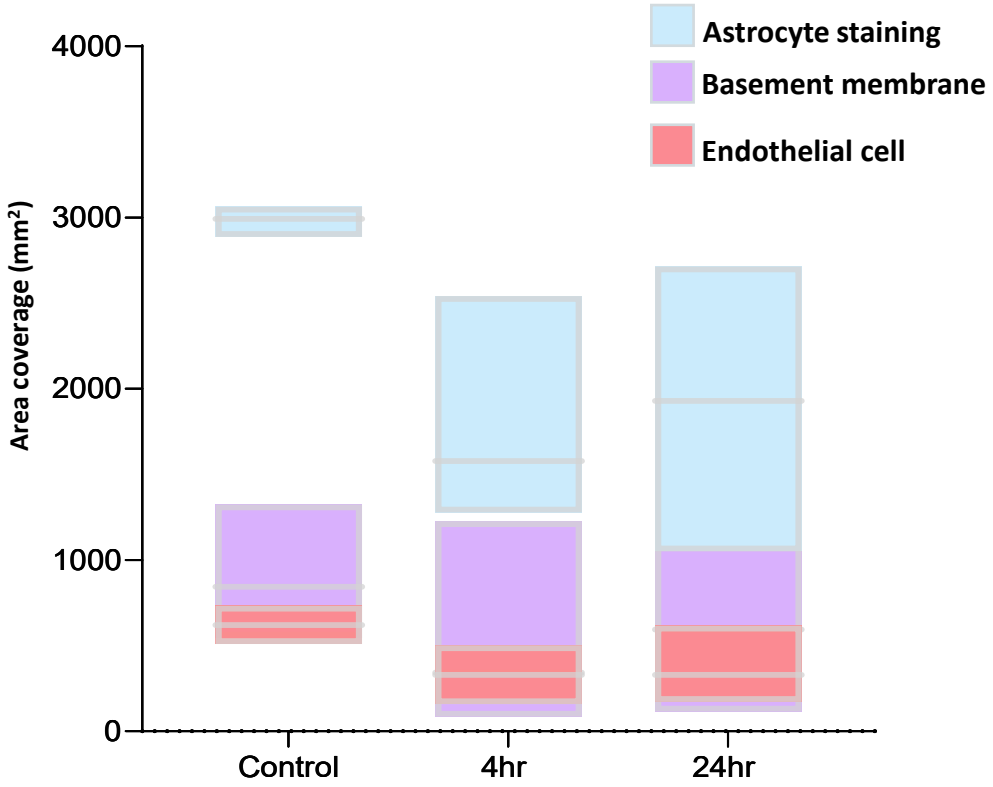




- BBB component/support cell coverage is reduced at 4&24hrs compared to control
- Alterations to these cells alter the structure and function of BBB detrimentally



Clinical relevance


Astrocyte staining
Basement membrane
Endothelial cell
Area coverage (mm²)
4000
3000
2000
1000
0
Control
4hr
24hr

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