BBB Disruption post TBI in SIRPα-KO Mice

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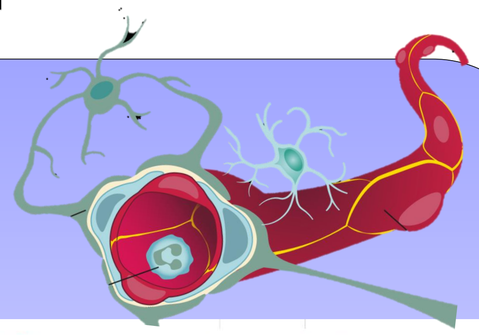
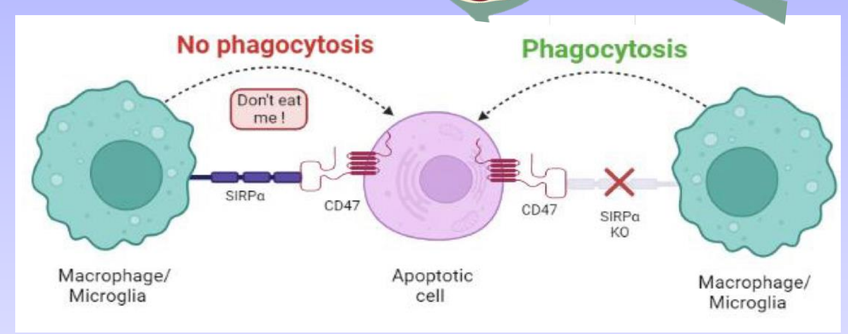
Introduction



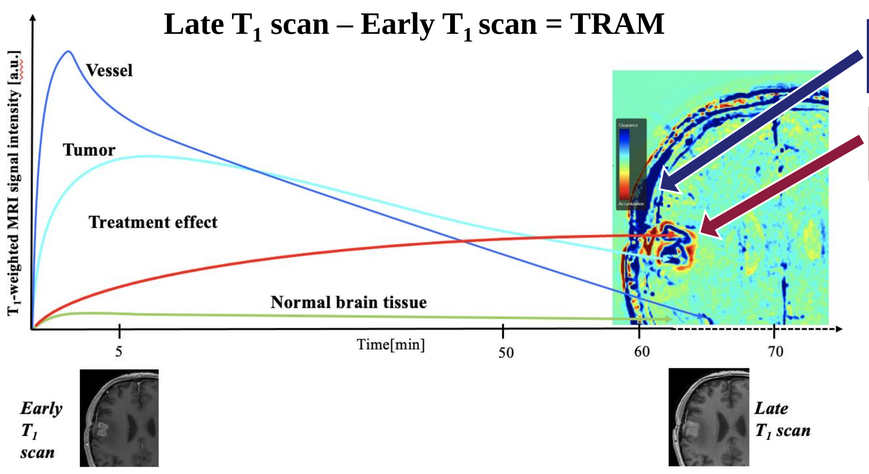
- **Traumatic Brain Injuries (TBI)** are the leading cause of death and disability in young adults and children in the developed world (Shlosberg et al., 2010)
- **The Blood-Brain Barrier (BBB)** can be damaged and leak post TBI (Shlosberg et al., 2010)
- **Microglia cells** are recruited as part of the brain's neuroinflammatory response (Cherry et al., 2014)
  - **Type M1:** upregulates inflammation, beneficial but can become harmful when out of control
  - **Type M2:** downregulates inflammation
- **Sirp-α receptor:** prevents type M2 microglia from using phagocytosis to "eat" the body's own cells.
  - **Sirp-α KO** → Upregulation of phagocytosis → M1 microglia homeostasis → Improved healing (Elberg et al., 2019)



Hypothesis

Sirp-α KO has a beneficial effect on the post-TBI permeability of the Blood Brain Barrier.

1 Methods I - Delayed Contrast MRI



Blue = Contrast Clearance

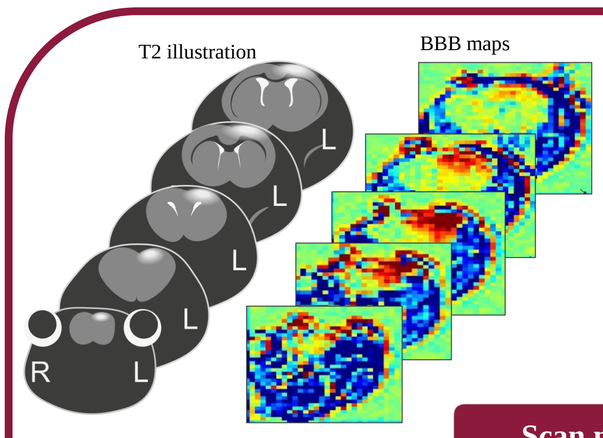
Red = Contrast Accumulation

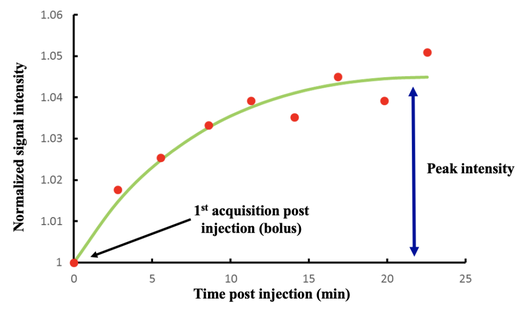
Blue – low levels
- Blood vessels, contrast agent is flushed out faster

Green – neutral levels
- Brain tissue

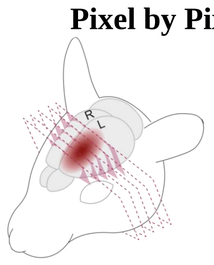
Red – high levels
- Damage in the BBB causes a leak

2 Methods II - Analysis



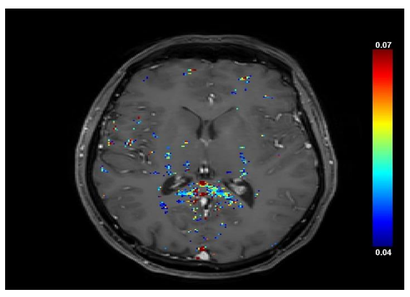


Pixel by Pixel



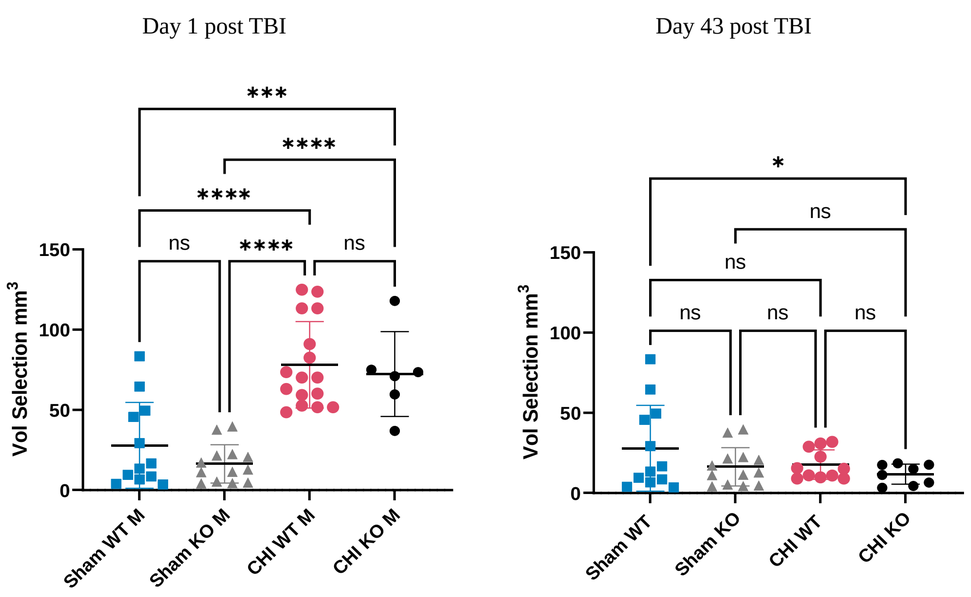
Scan me!

Mean Dynamic Peak

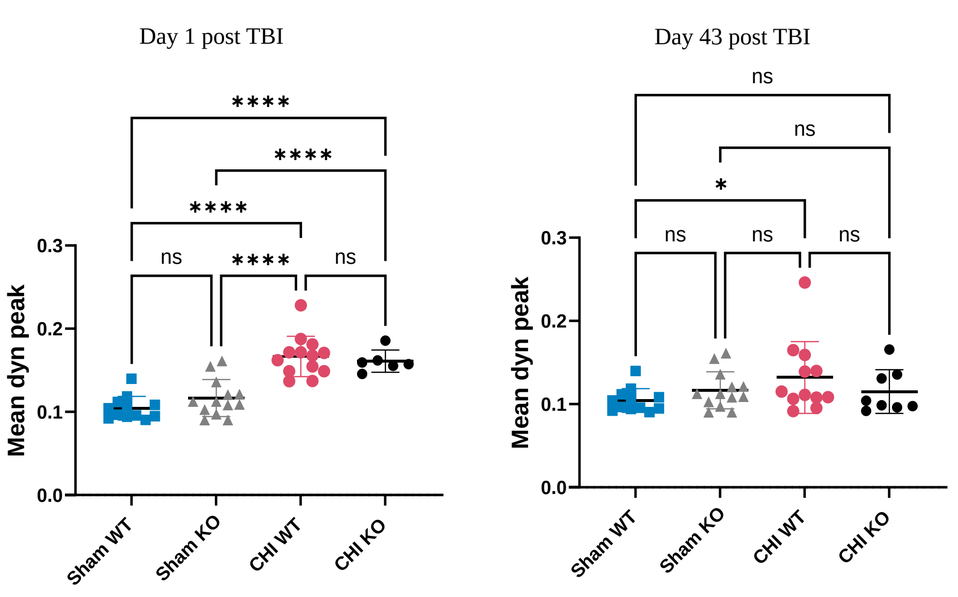


Results

Volume of BBB disruption in Sirp-α KO
(n=47 , male and female animals)



Intensity of BBB disruption in Sirp-α KO
(n=47 , male and female animals)



Conclusion

Sirp-α KO has no protective properties according to volume measurements.

Sirp-α KO might benefit healing as shown by the non-significant difference on day 43 in the intensity measures between the KO groups.

A limitation was caused by the low number of animals in the CHI-KO group.

Medical Applications

Use of delayed contrast MRI can improve TBI detection
BBB leakage often goes unnoticed in emergency room patients due to limitations of imaging methods.

Prevention of neurodegenerative diseases and other long-term consequences of TBI is achievable through more effective treatment methods.

Cherry, J. D., Olschowka, J. A., & O'Banion, M. K. (2014). Neuroinflammation and M2 microglia: The good, the bad, and the inflamed. *Journal of Neuroinflammation*, *11*(1), 98.
Elberg, G., Liraz-Zaltsman, S., Reichert, F., Matozaki, T., Tal, M., & Rotshenker, S. (2019). Deletion of SIRPα (signal regulatory protein-α) promotes phagocytic clearance of myelin debris in Wallerian degeneration, axon regeneration, and recovery from nerve injury. *Journal of Neuroinflammation*, *16*(1), 277.
Israeli, D., Tanne, D., Daniels, D., Last, D., Shneor, R., Guez, D., Landau, E., Roth, Y., Ocherashvilli, A., Bakon, M., Hoffman, C., Weinberg, A., Volk, T., & Mardor, Y. (2010). The Application of MRI for Depiction of Subtle Blood Brain Barrier Disruption in Stroke. *International Journal of Biological Sciences*, *7*(1), 1–8.
Shlosberg, D., Benifla, M., Kaufer, D., & Friedman, A. (2010). Blood-brain barrier breakdown as a therapeutic target in traumatic brain injury. *Nature Reviews. Neurology*, *6*(7), 393–403.