

# Longitudinal evaluation of blood-brain barrier pathology following experimental mild-TBI in swine

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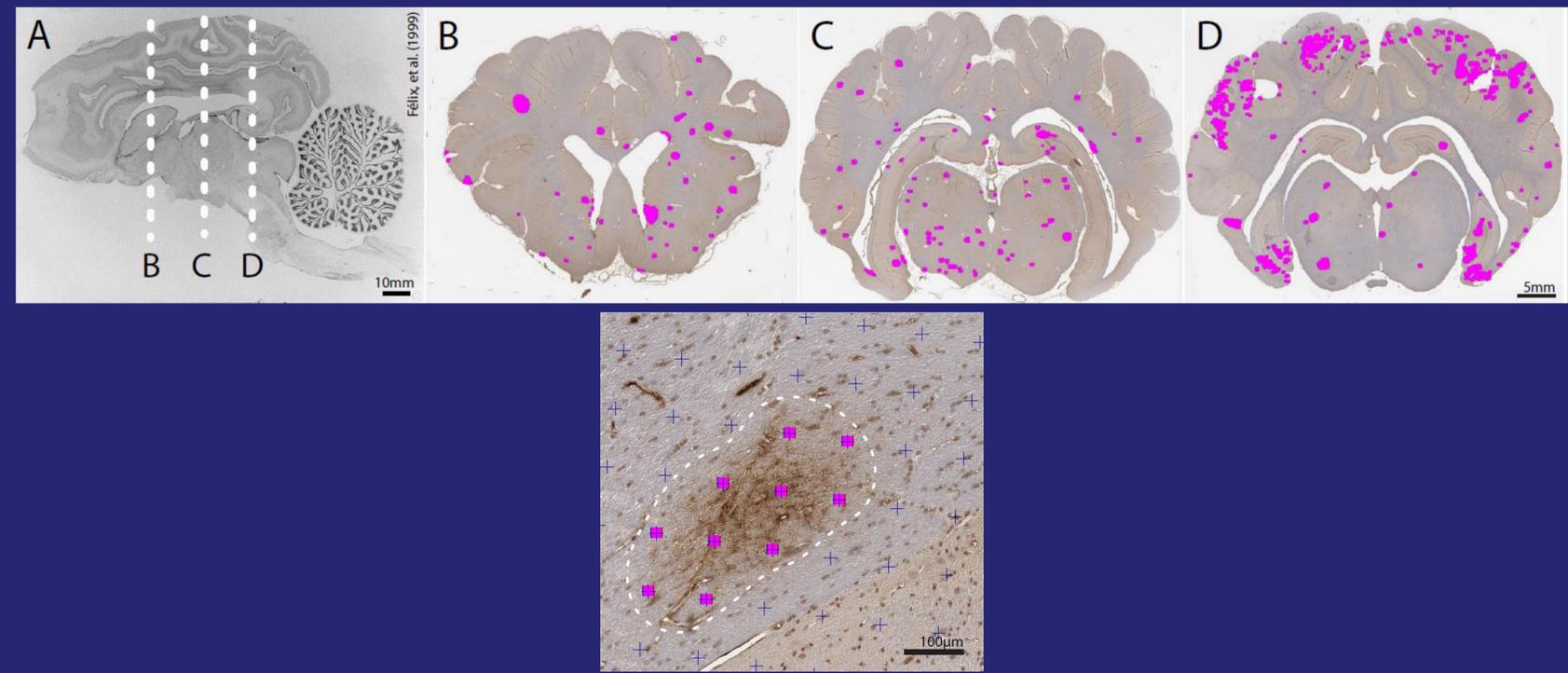
**Objectives:**  
 Blood-brain barrier (BBB) pathology is a well characterized diffuse pathological consequence of severe traumatic brain injury (TBI), which has been shown in autopsy studies to persist chronically in more than half of severe TBI survivors. Recently, members of our team demonstrated acute mechanical BBB disruption following experimental single mild-TBI (mTBI) in swine. However, the duration of overt BBB pathology in single mTBI is currently unknown. Using our one-of-a-kind non-impact swine rotational acceleration injury (RAI) TBI model, we sought to longitudinally evaluate the extent of BBB pathology following single mTBI.

**Design:**  
 As an initial first step, we performed immunohistochemical analysis on available tissue from our team's swine mTBI archive. A total of 15 animals were available for analysis which all underwent single RAI mTBI in the coronal plane, divided into the following four subgroups based on survival time post-mTBI: A) 3-days survival, n=4; B) 1-month survival, n=3; C) 1-year survival, n=3; D) SHAM control mTBI, n=5. Whole-brain coronal sections from three brain levels for each animal were subjected to immunostaining for serum fibrinogen, and the extent of resulting fibrinogen extravasation was quantified by determining the total volume of fibrinogen extravasation into the brain parenchyma as compared to the total volume of brain tissue analyzed across all three brain regions, generating a BBB leakage ratio (BBB-LR) for each animal.

**Results:**  
 Consistent with our teams prior acute BBB analysis, there was extensive fibrinogen extravasation observed 3 days post-mTBI (BBB-LR of 0.054 +/- 0.013). This was followed by a marked decrease in fibrinogen extravasation (BBB-LR of 0.008 +/- 0.007) 1-month post-mTBI, which remained constant out to 1-year post-mTBI (BBB-LR of 0.007 +/- 0.009), as was not statistically different from the SHAM controls (BBB-LR of 0.006 +/- 0.007).

**Conclusions:**  
 Our preliminary results indicate effective repair of the BBB by 1-month post- single mTBI in our experimental swine RAI model.

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**Resolution of overt blood-brain barrier pathology occurs within 1-month following single mTBI**, as evidenced by quantifying intraparenchymal fibrinogen extravasation in a clinically-relevant swine model of diffuse, non-impact rotational acceleration injury mTBI.

