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# Male and Female Mice Exhibit Divergent Responses of the Cortical Vasculature to Traumatic Brain Injury

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## Background

Traumatic brain injuries (TBI) occur in 1.7 million people each year in the USA. Little is known about how the cerebrovasculature is altered after TBI. We previously reported that TBI elicits acute decrements in cerebral vessels near the injury site in rats followed by revascularization over the subsequent 2 weeks. Sexual dimorphism of the brain is well documented and different hormonal levels in males and females differentially modify the recovery process after injury. However, the effects of biological sex on the temporal evolution of revascularization following TBI are understudied. Using a model of controlled cortical impact in male and female mice, we set out to determine if the injury and the repair process are affected by sex.

## Methods

Lesion volume was assessed using MRI T2-weighted imaging at 1 and 7 days post-injury (dpi). To evaluate the vascular

network, we used a new “vessel painting” technique that uses a fluorescent dye (DiI) to stain blood vessels. Vessel numbers and complexity were analyzed using the Angiotool software and Fraclac (ImageJ plugin). Blood-brain barrier (BBB) alteration, neurodegeneration, inflammation and endothelial activation were assessed through immunohistochemistry.

## Results

We found no sex differences in lesion volume, BBB alteration or neurodegeneration. However at 1 dpi, females exhibited more astrocytic hypertrophy, whereas males presented with increased endothelial activation and expression of beta-catenin, which has been shown to be involved in angiogenesis. At 7 dpi, we observed an increase in the number of vessels and an enhancement in vessel complexity in injured cortex of males compared to females.

## Conclusions

Our study suggests vascular repair mechanisms between males and females after TBI are likely different, highlighting the fact that consideration of sex is a critical step towards precision medicine. Further studies are needed to determine if these sex differences are beneficial or deleterious.

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