Inflammation and Oxidative Stress in Animal Models of Hydrocephalus

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Abstracts will be considered for both poster and platform presentations

Child neurology

Introduction
One consequence of preterm birth is neonatal intraventricular hemorrhage (IVH) which can lead to hydrocephalus. Although extravascular blood induces neuroinflammation, the mediators, time course and consequences of neuroinflammation after neonatal IVH are unknown. Oxidative stress leads to cell death in numerous models of neurological disease and progenitor cells that are present in the neonatal brain are especially susceptible to oxidative stress. The interplay of inflammation, oxidative stress and hydrocephalus is not well-studied.

Methods
We utilized rodent models of intraventricular hemorrhage and hydrocephalus. A meso-scale detection ELISA was used to quantify nine different inflammatory cytokines and Western blot was used to measure oxidative stress in the ipsilateral and contralateral hemispheres at 3,6 and 24 hours after IVH. Neurobehavioral testing was conducted using the Morris water maze. A mouse genetic model of hydrocephalus was used to study neuroinflammation in hydrocephalus without IVH.

Results
Numerous pro-inflammatory cytokines including TNFa are significantly elevated up to 200-fold from baseline levels acutely after IVH, and then return towards baseline within 24 hours. Markers of oxidative stress gradually increase with IVH with levels over 3-fold that of uninjured controls. Both inflammatory cytokine production and oxidative stress are present throughout the brain parenchyma and are not localized only to areas near the site of IVH induction. In animals with congenital hydrocephalus, neuroinflammation was present in areas of tissue injury near the ventricles. In this area, the activation of pathological macrophage activation was more robust than protective macrophage activation.

Conclusion
IVH causes a rapid wave of inflammation throughout the brain followed by an increase in oxidative stress. This indicates that both anti-inflammatory and anti-oxidant therapies may hold promise for treating children with IVH, but that these treatments might need to be applied at different time points to be effective. Inflammation also plays a role in congenital hydrocephalus, and may contribute to tissue injury.