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**Intraventricular hemorrhage induces rapid intracellular signaling in the choroid plexus and chronic changes in CSF reabsorption**

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**Introduction:**

Intraventricular hemorrhage (IVH) leads to acute hydrocephalus in a subset of preterm infants by unclear mechanisms that potentially include increased CSF production by the choroid plexus (ChP), based on recent work in adult rats (Karimy et al., 2017). The earliest physiologic changes within ChP epithelial cells likely involve calcium signaling, which is a known intracellular messenger in other secretory epithelial cell populations. The following experiments utilize rapid calcium imaging to evaluate how the calcium signaling pathway is regulated in embryonic ChP explants. We subsequently characterize chronic changes in this model of compensated hydrocephalus by measuring the intracranial compliance and resistance to CSF reabsorption.

**Methods:**

1. Calcium imaging of embryonic explants: Lateral ventricle choroid plexus is dissected at embryonic day 14.5 (E14.5) from a conditional transgenic mouse line (FoxJ1-Cre; Gcamp6f). The choroid plexus explants are exposed to focal blood injections and imaged for calcium responses using epifluorescence and two-photon imaging.
2. Intracranial compliance and resistance to CSF outflow measurements: a modified external ventricular drain is used to quantify intracranial pressure during infusion of artificial CSF in 2 month old post-IVH mice.

**Results:**

Upon exposure to age-matched embryonic plasma, nearly all ChP epithelial cells rapidly release highly concentrated intracellular calcium followed by a mosaic pattern of recurrent calcium release. Using different conditions of calcium blockade, we identify endoplasmic reticulum storage as the primary source of intracellular calcium release. Outflow resistance of CSF decreases in the chronic state, suggesting later compensation for the increased amount of CSF production.

**Conclusion:**

IVH causes immediate intracellular calcium release by the choroid plexus epithelia and delayed compensation for increased CSF production after one month. Together, these data highlight rapid and temporally dynamic changes in the intraventricular compartment and contribute to our understanding of IVH-induced hydrocephalus pathophysiology.