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**Abstract title:** Pilot Study of Cortical Dysfunction and Neuron Survival in Prenatal Hypoxic Insult

**Background:** Hypoxic ischemic-encephalopathy (HIE) from global perinatal hypoxia is a significant worldwide cause of neonatal morbidity and mortality, resulting in multiple neurodevelopmental diseases. Children with HIE demonstrate decreased gray matter volume and have a higher incidence of epilepsy. In postnatal HIE models, significant cell death from apoptosis has been described within 24 hours of insult. However, cell death has not been described in models of prenatal hypoxia. Therefore, we have developed a model of prenatal hypoxic insult to determine the effect of intrapartum oxygen deprivation on cortical volume, neuronal survival, and seizure threshold.

**Objective:** The purpose of this study is determine if mice exposed to prenatal hypoxic insult have neuroanatomical or functional evidence of abnormal cortical network abnormalities.

**Study Design/Methods:** Pregnant C57Bl/6N mice were exposed at E17.5 to 8 hours of normoxia or hypoxia (5% FiO<sub>2</sub>) via Biospherix hypoxia chamber. To assess for brain atrophy, ex vivo MRI of brains from adult mice from prenatal exposures were performed to obtain a T2-weighted sequence and whole brain volume was calculated. The seizure threshold of adult mice from prenatal exposures was assessed using flurothyl, an inhaled GABA antagonist that was infused into a sealed chamber. Mice were videotaped and time to first generalized tonic clonic seizure was determined by a blind observer. TUNEL staining for DNA fragmentation from apoptosis was performed on fetal brains harvested 24 hours after exposure. TUNEL positive cells were counted by a blinded observer.

**Results:** Preliminary data suggest less brain volume in hypoxic mice compared to control animals by histology and MRI. Preliminary data also indicate that adult mice exposed to prenatal hypoxic insult tend to seize more rapidly than control mice, suggesting decreased seizure threshold. However, TUNEL assay demonstrated no increase in cell death in fetal brains exposed to prenatal hypoxia.

**Conclusions:** There does appear to be a decrease brain volume that can be attributed to gray matter loss in adult mice exposed to prenatal hypoxia compared to normoxia. This is correlated with a decreased seizure threshold seizure, indicating functional cortical network dysfunction. Interestingly, cell death does not appear to be a significant contributor to decreased gray matter volume. Therefore, other mechanisms may be accounting for this volume loss, such as decreased dendritic complexity. Current studies are focused on repeating these studies and determining if neurons from mice exposed to prenatal hypoxic insult have decreased dendritic spine density.