

1. OVERVIEW/ABSTRACT

Hypoxic ischemic encephalopathy (HIE) is a common form of neonatal encephalopathy occurring after a period of compromised oxygen delivery to the brain during the perinatal period. It is a devastating birth complication associated with significant mortality and long-term, permanent neurodevelopmental impairment. Although the significant adverse consequences of HIE have been well established, there are currently no pharmacologic therapies available to treat affected newborns. Therapeutic hypothermia is the current standard of care for babies with moderate to severe encephalopathy from HIE, but this specialized therapy has strict eligibility criteria, is not an option for babies with mild symptoms, and is not readily accessible to all affected infants worldwide. Our proposed research program modeling hypoxic injury in larval zebrafish provides a novel system for studying the neurodevelopmental effects of early hypoxic injury and a robust, high throughput method for screening potential pharmacologic therapies. Specifically, we aim to study the role of individual NMDA Receptor (NMDAR) subunits in the hallmark excitotoxicity observed in patients with HIE and assess the efficacy of specific NMDAR subunit antagonists in providing neuroprotection. This unique effort brings together investigators from the Departments of Pediatrics and Neurobiology & Behavior in a collaborative research program with clear basic and translational relevance. Establishment of this animal model would facilitate identification of efficacious pharmacologic compounds for testing in clinical trials and is a necessary step in improving neurodevelopmental outcomes in newborns with HIE.