**Purpose:** To determine whether inhibition of NADPH oxidase (NOX) could ameliorate oxidative brain injury following cerebral hypoxic/ischemic (HI) injury in the neonatal rat.

**BACKGROUND:** Oxidative injury accompanies HI injury. Since very little recruitment of neutrophils occurs in neonatal HI (1), we sought an alternative source for oxy-radicals and established uncoupling of nitric oxide synthase (NOS) as a potential mechanism (2). NOS uncoupling results from a dysfunctional enzyme in which superoxide radical is generated in lieu of nitric oxide. Pharmacological inhibition of NOX with apocynin ameliorated uncoupling, potentially through sparing of oxidative depletion of cofactors. NOX inhibition decreases cerebral injury from ischemia (3). Here we investigate whether NOX inhibition also ameliorates oxidative brain injury.

**DESIGN/METHODS:** Seven day old neonatal rats (P7 rats) were subjected to HI by ligating one common carotid artery under anesthesia and exposure to 8% oxygen for 90 minutes followed by resuscitation with 100% oxygen for 2 hours. Pups were then given an intraperitoneal injection of a carrier solution or apocynin, 25 mg/Kg. After a survival of 24 hours, pups were euthanized, and cortical tissue from both sides of the brain was homogenized. Samples were assayed for lipid oxidation products using a TBARS assay and for nitrotyrosine using an ELISA assay.

**RESULTS:** TBARS reactive products and nitrotyrosine were increased (120% and 500% respectively) in cerebral hypoxic-ischemic cerebral tissue. There was a significant decrease in TBARS reactive products (54%; p = 0.035, n = 5) and nitrotyrosine (32%; p = 0.022, n = 5) in hypoxic-ischemic tissue of pups treated with apocynin.

**CONCLUSIONS/RELEVANCE:** Inhibition of NOX following H/I injury was able to ameliorate oxidative damage to lipids and proteins, suggesting that NOX activation participates in the oxy-radical cascade that accompanies this condition. Further studies are in progress to determine the effect of this treatment on structural and functional outcome measures.

**References:**

This work was supported by NICHD Grant HD39833

Category - Cerebrovascular Disease