Neurologic dysfunction in a pediatric porcine model of carbon monoxide poisoning

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Abstract

Our overarching goal for this CEET application is to advance understanding of pediatric neurological dysfunction from carbon monoxide (CO) poisoning using a robust large animal model. CO poisoning remains a major cause of death and disability, affecting approximately 75,000 people each year in the United States alone. Specially in the pediatric population, the effects of CO are less well-known and due to ongoing brain development of children, the mechanism of CO is not well- established and represents an important gap in knowledge. Another existing gap is the lack of effective biomarkers to gauge severity, prognosis, and response to treatment. While a carboxyhemoglobin (COHb) level is readily available at most institutions, its use is limited only to confirm exposure with no predictive value. The two main objectives our CEET proposal seeks to address are: (1) limited mechanistic understanding of the key role the mitochondria has in CO poisoning and (2) limitations of current biomarkers to gauge severity of disease and treatment response. This project will define the mitochondrial pathways of the brain involved in CO poisoning, a high-energy organ most effected in CO poisoning, and compare to circulating blood cells; thus, furthering the mechanistic understanding and developing a therapeutic blueprint for interventions.