Prolonged oxygen exposure causes long-term deficits on hippocampal mitochondrial function in newborns

October 15 2019

Credit: CC0 Public Domain

Findings recently published in *Nature Scientific Reports* by the University of Alabama at Birmingham's Manimaran Ramani, M.D., indicate that in

a rodent model prolonged oxygen exposure during the critical developmental period permanently impairs long-term hippocampal mitochondrial function.

Children and adolescents born preterm who require prolonged oxygen therapy in the neonatal intensive care unit often develop cognitive deficits, attention deficit disorder and autism spectrum disorder.

The exact mechanism by which children and adolescents born preterm develop cognitive and behavioral disabilities is not known. Previously, Ramani, an associate professor in the Division of Neonatology, and his team showed that young adult mice that are exposed to oxygen as newborns develop memory deficits and hyperactivity, findings similar to that of adolescent born preterm.

Although mitochondrial dysfunction and oxidative stress are associated with the pathogenesis of several neurodegenerative disorders such as Parkinson disease, the impact that early oxidative stress and mitochondrial dysfunction have on neurodevelopment is yet to be determined.

The hippocampus is the region of the brain that plays a key role in the formation and maintenance of long-term memory and is highly vulnerable to oxidative stress. Neurons in the hippocampus are dependent on their mitochondrial function for the strengthening of synapses, a cellular response responsible for long-term memory. This is the first preclinical study shows that early life oxygen exposure has a permanent negative impact on hippocampal mitochondria.

In their mouse model in which mice pups are exposed to oxygen, Ramani's team expected a recovery in hippocampal mitochondrial function when assessed at young adult age. On the contrary, the team was surprised by the fact that hippocampal mitochondrial dysfunction

persists even after the initial oxidative stress is long gone.

"Premature infants require oxygen supplementation for their survival and maintaining lower oxygen saturation is known to increase mortality," Ramani said. "Hence, research going forward should focus on determining the role of other modalities of therapies such as antioxidants to counteract the toxicity effects of oxygen."

More information: Manimaran Ramani et al. Early Life Supraphysiological Levels of Oxygen Exposure Permanently Impairs Hippocampal Mitochondrial Function, *Scientific Reports* (2019). DOI: 10.1038/s41598-019-49532-z

Provided by University of Alabama at Birmingham