Prolonged oxygen exposure causes long-term memory deficits for preterm infants

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Research findings in an article recently published in *Nature Scientific Reports* by University of Alabama at Birmingham neonatologists indicate that oxygen exposure in newborn mice pups impairs the signaling

pathways required for long-term learning and memory formation.

Preterm infants who require prolonged periods of oxygen supplementation are at a higher risk for developing neurodevelopment impairment. However, it is still not clear how oxygen supplementation in preterm infants, a need for survival in this patient population, can also be leading to deficits in long-term cognitive function.

To understand the long-term effect early oxygen exposure on the brain development, Manimaran Ramani, M.D., assistant professor in the UAB's Division of Neonatology, and his team developed a novel mouse model in which the newborn mice pups are exposed to neither oxygen nor room air for the first two weeks after birth, and then studied their cognitive function when they turned adolescents. Since the brain development in the newborn mice pups corresponds to that of 24- to 28-weeks of gestation in human preterm infants, this unique mouse model enables Ramani's research team to understand and develop therapies for early oxygen induced long-term cognitive dysfunction. In this model, adolescent mice that had oxygen exposure as neonates had spatial navigation memory deficits and hippocampal shrinkage—findings that are consistent with children born preterm.

"We are trying to identify therapeutic strategies to prevent and treat cognitive deficits seen in children born preterm and to understand the long-term effects of early oxygen exposure on brain development and function," said Ramani, lead author of the paper. "This study shows that, in mice, oxygen exposure during critical developmental period may have a deleterious effect on the hippocampal signaling pathway and mitochondrial function—critical needs for the memory formation and maintenance."

Ramani says additional studies will be needed to evaluate the strength of synaptic connections of the hippocampus and to determine the

mechanisms by which early oxygen exposure leads to mitochondrial dysfunction in the hippocampus, a brain region that plays an essential role in the formation and maintenance of memory.

"What this tells us is that oxygen supplementation during the newborn period may have a negative impact long-term brain function," Ramani said. "Since reducing oxygen supplementation is shown to increase the mortality among the preterm infants who require oxygen supplementation, we need to identify the therapies that can mitigate toxic effects of oxygen on brain development and function."

More information: Manimaran Ramani et al. Supraphysiological Levels of Oxygen Exposure During the Neonatal Period Impairs Signaling Pathways Required for Learning and Memory, *Scientific Reports* (2018). DOI: 10.1038/s41598-018-28220-4

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