Lack of oxygen, not blood flow, delays brain maturation in preterm infants

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Stephen Back, M.D., Ph.D., Clyde and Elda Munson Professor of Pediatric ResearchandPediatrics, OHSU School of Medicine, OHSU Doernbecher. Credit: OHSU/Kristyna Wentz-Graff

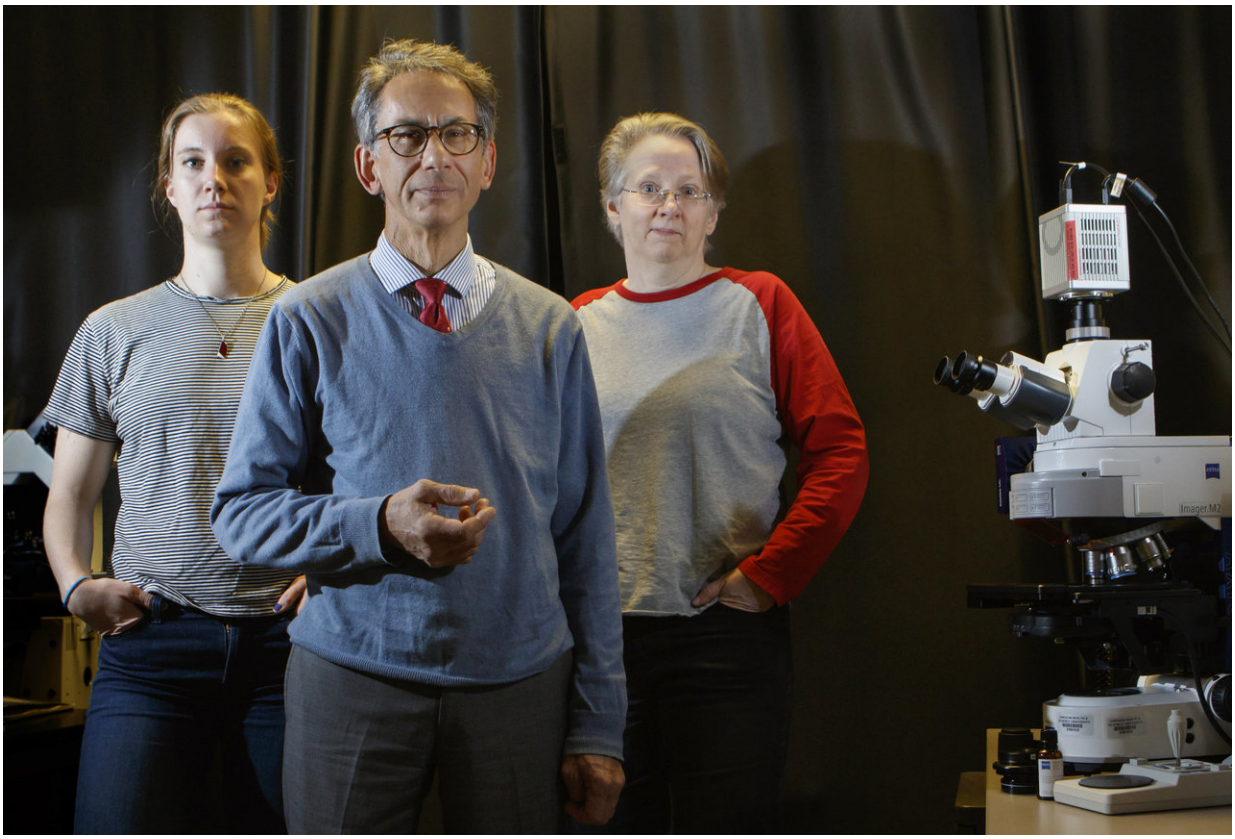
Premature infants are at risk for a broad spectrum of life-long cognitive

and learning disabilities. Historically, these conditions were believed to be the result of lack of blood flow to the brain. However, a new study published in the *Journal of Neuroscience*, finds that while limited blood flow may contribute, major disturbances are actually caused by low oxygen.

This research challenges more than a decade of scientific study and clinical understanding of brain development in preterm children, said the study's principal investigator Stephen Back, M.D., Ph.D., Clyde and Elda Munson Professor of Pediatric Research and Pediatrics, OHSU School of Medicine, OHSU Doernbecher.

"Previously, we thought lack of blood flow was causing preterm brain cells to die. Instead, these critically important cells simply fail to develop normally. This finding creates an opportunity to determine ways to restore oxygen loss and potentially reduce life-long impacts of preterm survivors."

Utilizing a preterm sheep model, Back and his team analyzed the response of fetal subplate neurons - cells that play a critical role in regulating preterm brain function and connectivity—to disturbances of brain oxygenation. When the developing brain was exposed to lower than normal rates of oxygen for as short as 25 minutes, subplate neurons showed major long-term disturbances just one month following exposure.



(Left to right) Kiera Degener-O'Brien, Stephen Back, M.D., Ph.D., and Ev McClendon analyzed the response of fetal subplate neurons to brain oxygenation disturbances. Their findings show lack of oxygen, not blood flow, delays brain maturation in preterm infants. Credit: OHSU/Kristyna Wentz-Graff

"This brief exposure to low oxygen occurs frequently in preterm babies receiving care in a neonatal intensive care unit," said Back. "And this result better explains the long-term complications that these preterm babies sustain as they grow older, which include significant challenges with learning, memory and attention."

Although additional research is needed to determine the exact developmental timeframes for potential injury due to oxygen loss in infants, as well as the optimal concentration of oxygen necessary for

early intervention therapies, Back believes these findings suggest a need to re-evaluate current practices in intensive care settings.

"Given this new range of opportunity to promote brain repair, clinicians must critically rethink how to interact with, stimulate and handle preterm babies during intensive care treatment. This will help to better manage transient low-oxygen states and determine what the preterm brain can and cannot tolerate."

More information: Transient Hypoxemia Chronically Disrupts Maturation of Preterm Fetal Ovine Subplate Neuron Arborization and Activity,*Journal of Neuroscience* (2017). www.jneurosci.org/content/earl… EUROSCI.2396-17.2017

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