Hope for infant brain injuries like cerebral palsy as well as multiple sclerosis

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(Medical Xpress) -- In a new study published in *Nature Neuroscience*, a team of researchers revealed the discovery of a key protein necessary for nerve repair and could lead to the development of a treatment for brain injuries due to a lack of oxygen, such a cerebral palsy, as well as multiple sclerosis, an autoimmune disease that affects adults all over the world.

David Rowitch from the University of California and his team studied the brains of young infants who had passed away due to an insufficient amount of oxygen to the brain. They discovered a gene known as AXIN2 is expressed in premature infants with white matter brain injuries. White matter brain injuries in infants occur when birth takes place prematurely and before lung development is complete. The lack of oxygen creates a disruption in the nerve cells ability to create myelin, or the protective coating found on nerves. Without this myelin, the brain cells die and can lead to cerebral palsy.

The researchers have also discovered this gene in patients with multiple sclerosis. In multiple sclerosis, the immune system, which normally fights off infections, turns on the body and attacks the myelin, leaving the nerves without the protective coating. They determined this AXIN2 protein is involved in certain cellular processes, with one being development.

Working with mice that had nerve damage in the white matter of the brain, the researchers injected a drug that stops the destruction of the AXIN2 protein into the areas of the mice brains that were myelin deficient. Once injected, these mice were able to regrow the myelin and repair the damage.

Although this arrested development of myelin producing cells has been seen in mice and patients with multiple sclerosis, there is no proof of this same condition in the brains of premature infants. While this discovery shows promise for a pharmaceutical target for re-growing myelin and repairing nerve damage in patients with multiple sclerosis, it is still unclear if this will be able to help treat infant brain injuries.

More information: Axin2 as regulatory and therapeutic target in newborn brain injury and remyelination, *Nature Neuroscience* (2011) doi:10.1038/nn.2855

Abstract

Permanent damage to white matter tracts, comprising axons and myelinating oligodendrocytes, is an important component of brain injuries of the newborn that cause cerebral palsy and cognitive disabilities, as well as multiple sclerosis in adults. However, regulatory factors relevant in human developmental myelin disorders and in myelin regeneration are unclear. We found that AXIN2 was expressed in immature oligodendrocyte progenitor cells (OLPs) in white matter lesions of human newborns with neonatal hypoxic-ischemic and gliotic brain damage, as well as in active multiple sclerosis lesions in adults. Axin2 is a target of Wnt transcriptional activation that negatively feeds back on the pathway, promoting ?-catenin degradation. We found that Axin2 function was essential for normal kinetics of remyelination. The small molecule inhibitor XAV939, which targets the enzymatic activity of tankyrase, acted to stabilize Axin2 levels in OLPs from brain and spinal cord and accelerated their differentiation and myelination after hypoxic and demyelinating injury. Together, these findings indicate that Axin2 is an essential regulator of remyelination and that it might serve as a pharmacological checkpoint in this process.