Oxygen improves blood flow, restores more function in spinal cord injuries

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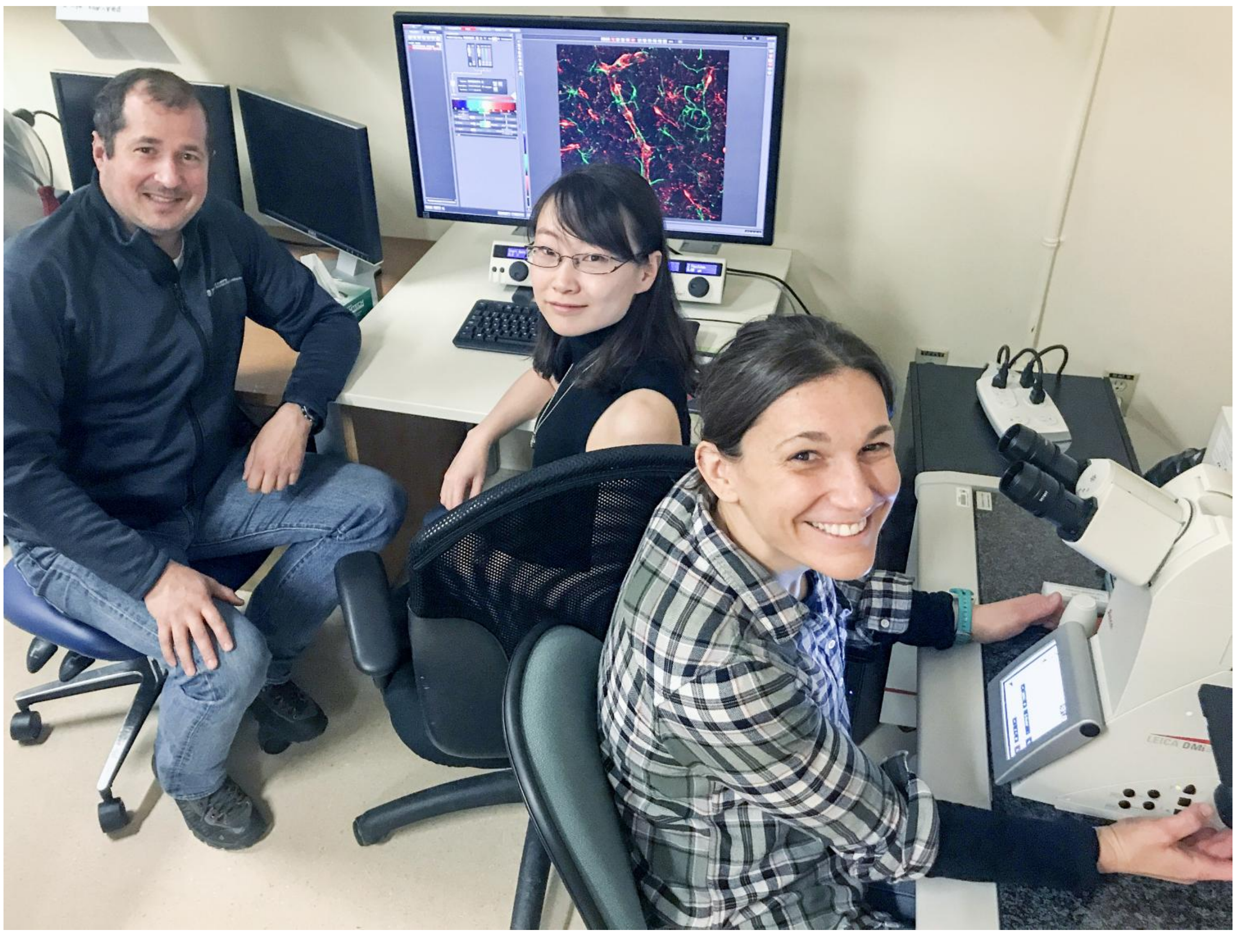

Karim Fouad and post-doctoral fellows Yaqing Li (center) and Ana M. Lucas-Osma (right) and their team made a new discovery that could alter how we view spinal cord function and rehabilitation after spinal cord injuries. Credit: Laurie Wang, University of Alberta

A new discovery at the University of Alberta will fundamentally alter how we view spinal cord function and rehabilitation after spinal cord injuries. Neuroscientists found that spinal blood flow in rats was unexpectedly compromised long after a spinal cord injury (chronically ischemia), and that improving blood flow or simply inhaling more oxygen produces lasting improvements in cord oxygenation and motor functions, such as walking.

Previous work had shown that while blood flow was temporarily disrupted at the injury site, it resumed rapidly, and it was more or less assumed that the blood flow was normal below the injury. This turns out to be wrong.

"We've shown for the first time that spinal cord injuries (SCI) lead to a chronic state of poor blood flow and lack of oxygen to neuronal networks in the spinal cord," says co-principal investigator Karim Fouad, professor, Faculty of Rehabilitation Medicine and Canada Research Chair for spinal cord injury. "By elevating oxygen in the spinal cord we can improve function and re-establish activity in different parts of the body."

Published in *Nature Medicine* on May 1, 2017, the study demonstrates chronic ischemic hypoxia (lack of blood and oxygen) after spinal cord injury and how blood flow plays a key role in the cause and treatment of motor disorders. Simply put, this could mean restored activity and ability in parts of the body that stopped working after spinal cord injury in the near future.

The discovery, like most "eureka moments" in science, happened by accident. The lead author Yaqing (Celia) Li, rehabilitation science post-doctoral fellow, and David Bennett, co-principal investigator and professor, Faculty of Rehabilitation Medicine, were looking at the injured spinal cord of a rat under a microscope and noticed the capillaries contracting in response to application of dietary amino acids like tryptophan.

"I thought, 'why would capillaries contract, when conventionally arteries are the main contractile vessels, and why should dietary amino acids circulating in the blood cause these contractions?'" says Bennett. "That is just plain weird, that what you eat should influence blood flow in the spinal cord." So they set out to answer these questions.

Li, Bennett and Fouad found that the AADC (Aromatic l-amino acid decarboxylase) enzyme that converts dietary amino acids into trace amines was upregulated in specialized cells called pericytes that wrap capillaries. Unexpectedly, these trace amines produced in the pericytes caused them to contract, clamping down on the capillaries and reducing blood flow. This surprising finding led them to make basic measurements of blood flow and oxygenation below the spinal cord, which led to the discovery of the chronic ischemic hypoxia. They reasoned that the capillaries were excessively constricted by these pericytes after SCI, since there is ample supply of tryptophan. So they decided to try blocking AADC to improve blood flow.

"Since blood flow below the injury is compromised, the neuronal networks function poorly with a lack of oxygen. So we blocked the AADC enzyme and found that it improved blood flow and oxygenation to the networks below the injury," Bennett says. "More importantly, this allowed the animals to produce more muscle activity."

As an alternative treatment to blocking the AADC enzyme in the spinal cord of rats, the neuroscientists exposed the animals to higher oxygen levels and even they were surprised to see what happened next.

"The rat could walk better!" Fouad says. "The change in oxygen restored function, albeit temporarily."

Though the team knows their discovery can have big implications in the world of neuroscience, rehabilitation and spinal cord injury, they are quick to mention a disclaimer.

"There is still a long way to go when it comes to treatment and helping patients with spinal cord injuries," says Fouad. "But this discovery has helped us understand the etiology of spinal cord injuries in a way we never did before. We can now design treatments that improve blood flow to produce long-term rehabilitation after SCI.

Possibly even simple therapies such as exercise or just breathing will play a role in preventing long-term hypoxia and damage to the spinal cord. It's a small but important step in the right direction, stemming from studying an obscure enzyme in the spinal cord—and that's the beauty of basic science."

More information: Pericytes impair capillary blood flow and motor function after chronic spinal cord injury, *Nature Medicine* (2017). nature.com/articles/doi:10.1038/nm.4331

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