Oligodendroglia cells protect neurons against neurodegeneration

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(Medical Xpress) -- Johns Hopkins researchers say they have discovered that the central nervous system's oligodendroglia cells, long believed to simply insulate nerves as they "fire" signals, are unexpectedly also vital to the survival of neurons. Damage to these insulators appears to contribute to brain injury in neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease for the Yankee baseball great who died from the disease.

The discovery, described online in the journal *Nature*, suggests that a previously unknown -- and unexpected -- function of these cells is to supply nutrition to the principal brain cells, neurons. This new pathway may prove to be an important and novel therapeutic target for ALS, the researchers say, and potentially other diseases that attack the body's nerve fibers, such as multiple sclerosis.

"More than 100 years after their discovery, we have now found a fundamentally new property in the way oligodendroglia work in the brain, laying the foundation for a new approach to try to treat debilitating neurodegenerative diseases," says Jeffrey D. Rothstein, M.D., Ph.D., a professor of neurology and neuroscience at the Johns Hopkins University School of Medicine, and the study's leader. "We've added a whole new category to what they do in the brain."

The cells responsible for the transfer of information and electrical impulses around the body, neurons work by transferring electrical charges from neuron to neuron. Axons, the wire-like extensions of the

neurons, help move the messages, in some cases over many feet, from cell to cell. Oligodendroglia insulate axons, like rubber coating around an electrical wire, to speed up the conduction of information. Axonal death is a hallmark of ALS and most other neurodegenerative disorders, Rothstein says.

Rothstein and his colleagues say the other principal brain cells, the astroglia, were believed to be primarily responsible for providing energy to neurons in the form of glucose, but their experiments show that oligodendroglia are surprisingly crucial in feeding neurons -- in the form of less energy-rich lactate, without which neurons and their axons die. Lactate has long been seen as a minor player in this process, but the Johns Hopkins team says it appears to be far more important to nerve cell survival. Moreover, they found that the protein MCT1, the dominant transporter of lactate in the brain, is only found in oligodendroglia.

Rothstein says their discovery was rooted in experiments during which scientists, using mice, knocked out the gene that makes the MCT1 protein and saw axons begin to die, even though they were still getting plenty of glucose.

As part of these experiments, the researchers engineered mice whose cells would light up if they were expressing MCT1. The scientists then determined that only oligodendroglia cells lit up, showing that MCTI is located on this type of cell alone. They also knocked out the MCT1 in cell cultures and found that neurons would begin to die, but would recover when fed lactate, proving the importance of MCT1 in providing this nutritional compound. They conducted the same experiments in mice and got similar results.

Finally, the researchers turned their attention to ALS, a disease where they had recently uncovered abnormalities related to oligodendroglia. In ALS mice, they found that MCT1 was missing in brain cells well before

the disease developed, and they found similar results in ALS patients. Rothstein says the findings suggest that oligodendroglia injury -- specifically injury to the mechanism that produces MCT1 -- may be an important event in the onset and progression of ALS.

Rothstein, who is director of the Johns Hopkins University School of Medicine's Brain Science Institute, says he hopes further research can establish that the activation of MCT1 in people will protect axons in those with ALS and other degenerative diseases.

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