Finding challenges accepted view of MS: Unexpectedly, damaged nerve fibers survive

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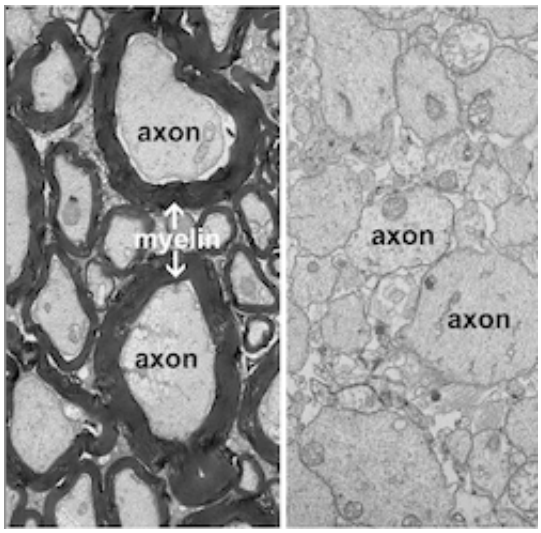

Spinal-cord tissue from normal (left) and mutant (right) rats. The normal tissue show a thick, effective layer of myelin insulation needed for normal nerve signaling. The mutant rats have no myelin, but surprisingly, the axons (long nerve fibers) remain intact. Credit: Chelsey Smith and Ian Duncan, UW-Madison

(Medical Xpress)—Multiple sclerosis, a brain disease that affects over 400,000 Americans, causes movement difficulties and many neurologic symptoms. MS has two key elements: The nerves that direct muscular movement lose their electrical insulation (the myelin sheath) and cannot transmit signals as effectively. And many of the long nerve fibers, called axons, degenerate.

Many scientists believe that axons are doomed once they lose the insulation, but a new study by graduate student Chelsey Smith and former undergraduate Elizabeth Cooksey in the *Journal of Neuroscience* shows axons can survive for long periods in rats even after losing myelin.

"This was the first study to demonstrate long-term axon survival after myelin deterioration," says senior author Ian Duncan, a professor in the School of Veterinary Medicine at the University of Wisconsin-Madison.

The mutant rats in the experiment have substantial myelin at first, but by eight weeks the essential myelin insulation is lost. "It was surprising," says Duncan, an expert in MS pathology. "Nine months is a relatively long period in a rat's lifetime, and there wasn't a loss of axons, so the assumption that axons must automatically die without myelin seems incorrect."

Normally, insulating myelin is made by supportive cells called oligodendrocytes that live alongside the axons. Duncan observes that oligodendrocytes and related cells also assist nerve cells by secreting growth factors that neurons may need to survive. "That is just speculation, but in our study, the oligodendrocytes were found in much greater numbers, probably in an attempt to produce more myelin, and we saw an overall increase in growth factor production."

Although oligodendrocytes definitely produce growth factors during early development in the rat, this study identified three neural growth factors that are produced by these helper cells in the older animals. "This paper was the first to show that oligodendrocytes continue to express growth factors in mature animals, and that could be important," Duncan says.

Growth factors are proteins that stimulate a wide range of growth and development, and their absence has been implicated in several neurological diseases. Duncan says more study of growth factors could suggest a route to preventing nerve fiber loss in MS and other myelin diseases.

Although other researchers have found that axons survive in mutant mice that fail to make myelin, Duncan notes that those animals lived only four months. "This survival was more than double that; it's a significant increase."

Scientists have known for decades that axons degenerate and disappear in MS, and that idea is now a major focus of scientific interest. "Much in vogue is the idea that you have to protect axons above and beyond everything else, that MS is not primarily a demyelinating disease, it's primarily an axonal disease," Duncan says. "Our finding shows that it is not absolutely certain that axons will degenerate when they are demyelinated. If we are correct in our speculation, we could potentially protect the axon if we can increase the amount of growth factor being produced by the helper cells."

Provided by University of Wisconsin-Madison