Improving recovery from spinal cord injury

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Once damaged, nerves in the spinal cord normally cannot grow back and the only drug approved for treating these injuries does not enable nerve regrowth. Publishing online this week in the Early Edition of the *Proceedings of the National Academy of Sciences,* researchers at the Johns Hopkins University School of Medicine show that treating injured rat spinal cords with an enzyme, sialidase, improves nerve regrowth, motor recovery and nervous system function.

"This is the first functional study showing behavioral improvement below a spinal cord injury by the delivery of sialidase," says Ronald Schnaar, Ph.D., a professor of pharmacology and molecular sciences at Johns Hopkins. "Sialidase has properties that are appealing from the human drug development point of view."

Sialidase is a bacterial enzyme that removes specific chemical groups found on the surface of nerve cells. The chemical groups normally function to stablize the cells, but also act to prevent nerve regeneration.

The team built upon earlier research where they disovered that sialidase treatment improved the growth of nerves into a graft. "We wanted to take this further and look at the animal model most relevant to human spinal cord injury," says Schnaar. "Typically, in motor vehicle accidents for example, vertebra shift and pinch the spinal cord, severing the long spinal nerve axons like you would if you pinched a piece of wet spaghetti." So they treated rats after a spinal cord impact injury by injecting sialidase directly to the injury site.

Rats with lower-back impact injury — severe enough to lose hind-limb function — were injected with sialidase directly over the spinal cord immediately following injury. The researchers then implanted into each rat a small pump that delivered a steady stream of sialidase directly to the injury over the course of two weeks, hoping that bathing the injured nerves in the enzyme would help their recovery and promote regrowth. They then let the rats recover for another three weeks before assessing the degree of recovery.

Using a well-established, 21-point scale where zero represents paralysis and 21 is normal function, the team of researchers assesed treated and untreated rats for a range of functions including whether they could lift their feet off the ground and whether they had coordinated leg movements. The initial injury rendered all rats to score below four, and all rats, treated or not, recovered somewhat by the end of two weeks. By the end of five weeks after injury most untreated rats scored 12 or less, while most treated rats scored better than 15. "The difference in coordination control was most remarkable," says Schnaar.

In addition to motor control, spinal cord injury can cause other nervous system problems, including losing the ability to control blood pressure and heart rate. To see if sialidase treatment improved nerve connections enough to remedy these problems, the team measured the nerve circuits that control blood pressure in treated and untreated rats. They found that treated animals improved blood pressure control. "We interpret this as improved communication in the spinal cord," says Schnaar.

Finally, the team looked at the nerve ends under a microscope and found that indeed, treated nerves showed an increased number of "sprouted" nerve ends, which according to Schnaar, provided anatomical evidence to add to the functional evidence that "something is going on."

"The positive is that we have shown functional recovery in a relevant

animal model of spinal cord injury," says Schnaar. "That being said, we haven't done full toxicity studies on these rats, which definitely needs to be done before we think about taking the long road into using this as a drug in people; efficacy in animals also doesn't necessarily translate to humans."

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