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Researchers reverse stroke damage by jumpstarting nerve fibers

December 7 2010

A new technique that jumpstarts the growth of nerve fibers could reverse much of the damage caused by strokes, researchers report in the Jan. 7, 2011 issue of the journal *Stroke*.

"This therapy may be used to restore function even when it's given long after ischemic brain damage has occurred," senior author Gwendolyn Kartje, MD, PhD and colleagues write.

The article has been published online in advance of the print edition of *Stroke*. Kartje is director of the Neuroscience Institute of Loyola University Chicago Stritch School of Medicine and chief of neuroscience research at Edward Hines Jr. VA Hospital.

There currently is little doctors can do to limit stroke damage after the first day following a stroke. Most strokes are ischemic (caused by blood clots). A drug called tPA can limit damage, but must be given within the first three hours for the greatest benefit -- and most patients do not receive treatment within that time window.

Kartje and colleagues report on a treatment called anti-Nogo-A therapy. Nogo-A is a protein that inhibits the growth of nerve fibers called axons. It serves as a check on runaway nerve growth that could cause a patient to be overly sensitive to pain, or to experience involuntary movements. (The protein is called Nogo because it in effect says "No go" to axons.) In anti-Nogo therapy, an antibody disables the Nogo protein. This allows the growth of axons into the stroke-affected side of the body and the

restoration of functions lost due to stroke.

Kartje and colleagues report dramatic results of anti-Nogo therapy in rats that had experienced medically induced strokes. Researchers trained rats to reach and grab food pellets with their front paws. One week after experiencing a stroke, the animals all had significant deficits in grabbing pellets with their stroke-impaired limbs. There was little improvement over the next eight weeks.

Nine weeks after their stroke, six rats received anti-Nogo therapy, four rats received a control treatment consisting of an inactive antibody and five rats received no treatment. Nine weeks later, rats that had received anti-Nogo therapy regained 78 percent of their pre-stroke ability to grab pellets. By comparison, rats receiving no treatment regained 47 percent of their pre-stroke ability, and rats receiving the control treatment of inactive antibodies regained 33 percent of their pre-stroke performance.

Subsequent examination of brain tissue found that the rats that received anti-Nogo therapy experienced significant sprouting of axons.

Researchers wrote that anti-nogo therapy "can induce remarkable compensatory sprouting and fiber growth, indicating the responsiveness of the chronically injured brain to form new neural networks under the proper growth conditions."

The findings "are of great clinical importance," researchers concluded. Anti-Nogo-A therapy "may benefit not only victims of spinal cord injury or patients in the early stage of stroke recovery, but also patients in later stages who suffer from neurological disability due to brain damage from stroke or other causes."

In a Phase I, multicenter trail at other centers, patients paralyzed by spinal cord injuries are receiving anti-Nogo therapy. The trial is

sponsored by the pharmaceutical company Novartis.

Provided by Loyola University