

# Treadmill training after spinal cord injury promotes recovery when inflammation is controlled

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New research suggests that treadmill training soon after a spinal cord injury can have long-lasting positive effects on recovery – as long as the training is accompanied by efforts to control inflammation in the lower spinal cord.

The study, in animals, also is among the first to show that [spinal cord injuries](#) can create impairments in parts of the cord located many spine segments away from the [trauma](#) site.

Researchers observed signs of [inflammation](#) in the lumbar region of the spine, at least 10 segments below the mid-[back injury](#), within 24 hours of the trauma. The health of the lumbar region is particularly important to recovery of lower-body movement because it contains important [circuitry](#) responsible for walking and other types of locomotion.

The study suggested that controlling inflammation is critical to the success of treadmill training.

Mice that received treadmill training just a few days after [injury](#) during a period of heightened inflammation got no lasting benefits. In contrast, animals trained on treadmills when inflammation was minimal regained the use of their [hind legs](#) to walk and retained those benefits for up to 42 days.

"We got positive and negative effects with the same intervention, and it's all influenced by inflammation," said D. Michele Basso, professor of health and [rehabilitation sciences](#) at The Ohio State University and senior author of the study. "There's so much happening so far away from the injury, and it's all in the heart of where the [neural circuits](#) are for locomotion."

The study showed that an enzyme called MMP-9 has a role in causing the lumbar inflammation. Because previous research has linked this enzyme to cancer, experimental drugs that inhibit it are already in the drug-development pipeline. Common [antibiotics](#) also could help control this type of inflammation, researchers say.

"The opportunity is there to begin to think about doing this in humans," Basso said.

The research is published in the Aug. 7, 2013, issue of *The Journal of Neuroscience*.

Basso's lab focuses on studying which activity-related interventions are most likely to improve recovery after a [spinal cord](#) injury. She also is a practicing physical therapist who provides treadmill training to patients, but usually months after the injury and in an outpatient rehabilitation setting.

So part of this study was geared toward understanding the window of time after injury that is best for treadmill training. With this intervention, patients' body weight is supported by a harness while therapists move their legs on a treadmill. The theory behind the technique is that sensory information coming from the legs to the lumbar spinal cord will allow nerve cells in this region to relearn how to walk – without needing input from the brain, because those signals are interrupted at the injury site.

The researchers added the inflammation component to the study based on the known properties of the MMP-9 enzyme. MMP-9 is involved in a number of central nervous system processes such as learning and plasticity, tissue remodeling and inflammation, and is regulated by exercise. But it also may create a toxic interaction after spinal cord injury.

Studying normal mice with thoracic spinal cord injuries, the researchers found five times more MMP-9 in the lumbar region seven days after the trauma as well as high levels of inflammation-related chemicals and changes in cell behavior. In contrast, mice that were genetically modified so they could not produce the MMP-9 enzyme had far fewer signs of inflammation in the lumbar region after the injury.

"We found neurovascular reactivity around locomotor networks, which suggests inflammatory processes are occurring 10 segments away from the injury. We've defined the role of MMP-9 in the lumbar cord as proinflammatory," said Christopher Hansen, a doctoral student in the Neuroscience Graduate Studies Program at Ohio State and lead author of the study. "This is significant, to be able to characterize the cellular microenvironment around networks that control locomotion.

"It's also new evidence that a thoracic injury can have effects on the motor system that is 10 or more segments away."

The researchers conducted early treadmill training on the same two types of animals: normal mice and mice that could not activate MMP-9. Control animals of both types received no exercise training.

Only mice deficient in MMP-9 showed significant improvements in walking on the treadmill with their body weight supported and also without any aid after seven days of training. These improvements lasted for four weeks. No other group of mice had the same results.

Researchers also tested the effects of late treadmill training, which started at least 35 days after the injury. The training failed to produce significant walking improvements in any of the animals.

"This was the exact same type of training, and in one group of mice the inflammation was controlled, but even in those mice the late training had no effect," Basso said. "We still don't know exactly when the window is for [treadmill training](#), but this suggests early, and with controlled inflammation. "

The scientists are continuing this work to further clarify the best timing for [treadmill](#) training and other exercise-based interventions, as well as other factors that affect the inflammatory response after a spinal cord injury.

Provided by The Ohio State University

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