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Spleen might be source of damaging cells at spinal cord injury site

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The spleen, an organ that helps the body fight infections, might also be a source of the cells that end up doing more harm than good at the site of a spinal cord injury, new research suggests.

Considering the spleen's role in the after-effects of spinal cord injury could change the way researchers pursue potential treatments for these devastating injuries.

In the days and weeks after the spinal cord is damaged, a variety of cells travel to the wound site. In a typical wound, such as a cut on the skin, cells like this cooperate to promote healing.

But the spinal cord environment is not typical. It is specialized tissue in a confined and delicate space. And when its own cells and other cells join to protect the wound, some cells end up promoting inflammation, which can exacerbate the effects of the injury.

Most research in this area has explored the bone marrow as a source of these pro-inflammatory cells, called macrophages, but some previous studies have suggested that the spleen is another source.

An Ohio State University study showed an overall 20 percent drop in the number of these macrophages two weeks after spinal cord injury in mice without a spleen when compared to injured mice that still had their spleens. The research suggests that the spleen might be a potential target for therapies designed to either inhibit release of these cells or alter their

function.

"The spleen is releasing cells that are traveling to the injury site and it's a significant number of cells," said Alicia Hawthorne, a postdoctoral researcher in neuroscience at Ohio State who led the study. "If we could target the spleen to decrease these cells or change their properties and make them less destructive, this might help promote the repair process as opposed to letting them cause inflammation or further damage to neurons."

Hawthorne presented the research in a poster session today (11/14) at the Society for Neuroscience annual meeting in San Diego.

The researchers compared the characteristics of spinal cord injury sites in two groups of mice: those whose spleens had been removed before the injury and those that still had their spleens. These injuries were in the T-9 region, roughly the middle of the back, and caused paralysis in the animals' hind limbs.

Fourteen days after the injury, the mice without spleens showed an overall 20 percent decrease in macrophage activity at the injury site compared to mice with their spleens.

To ensure the spleen was the likely source of these cells, the researchers also analyzed the characteristics of cells in the bone marrow, blood, spleen and spinal cord. They found that the spleen's cells were very similar to the cells circulating through the blood to the spinal cord site. The cells start out as monocytes, a different type of white blood cell, and then change into macrophages, which promote inflammation at the injury site.

The spinal cord itself is yet another source of macrophages at the injury site, but the researchers believe these so-called "resident" cells do more

good than harm. It's the intense peripheral cell immune response in spinal cord injury, where sensitive tissue and blood vessels are essentially ripped apart and form a traumatic wound, that the scientists someday hope to control in an effort to improve function after the injury.

Knowing more about the cells coming from the spleen could have important clinical implications. The spleen is seen as an excellent drug target, the researchers say, because it filters blood, making intravenous drug delivery easy and effective.

"If we can understand how these cells function and can understand the sequence with which they're released and migrate to the spinal cord, we can manipulate them. How do we manipulate them? That's something we don't know yet," said Phillip Popovich, professor of neuroscience, director of Ohio State's Center for Brain and Spinal Cord Repair and senior co-author of the study. "Understanding the dynamics of the cell population outside the central nervous system will improve our ability to control inflammation once it's triggered by a trauma."

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