

Neuroinflammation seen in spinal cord, nerve roots of patients with chronic sciatica

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A study by Massachusetts General Hospital (MGH) investigators has found, for the first time in humans, that patients with chronic sciatica—back pain that shoots down the leg—have evidence of inflammation in key areas of the nervous system. In their paper published in the May issue of the journal *Pain*, the research team reports finding that average levels of a marker of neuroinflammation were elevated in both the spinal cord and the nerve roots of patients with chronic sciatica. Additionally, the study showed an association between neuroinflammation and response to anti-inflammatory steroid injections, with levels of neuroinflammation differing between those whose pain was and those whose pain was not relieved by steroid injection treatment.

"Sciatica is an extremely common [pain](#) condition and is estimated to affect around 5 percent of men and 4 percent of women in their lifetimes," says Yi Zhang, MD, Ph.D., of the Center for Pain Management in the MGH Department of Anesthesia, Critical Care and Pain Management, a co-senior author of the report. "More than 5 million cases of [sciatica](#) are seen annually in the U.S., which represent a major cause of lost work days."

Several animal studies have documented activation of the immune system—including glial cells, which function as the immune cells of the nervous system—in chronic pain, raising the possibility that blocking neuroinflammation could be a viable treatment. Recent evidence from the laboratory of co-senior author Marco Loggia, Ph.D., of the MGH-

based Martinos Center for Biomedical Imaging, found glial cell activation in the brains of patients with chronic pain, but no prior studies have demonstrated neuroinflammation beyond the brain in humans with chronic pain. Even though a contribution of inflammation to acute pain in sciatica provides the rationale for anti-inflammatory steroid injections, evidence linking neuroinflammation with chronic sciatic pain in humans has been limited.

The current study combined both MR and PET imaging to test the hypothesis that chronic radiculopathy, a condition combining sciatica with additional lower-back-pain symptoms, would be associated with inflammatory activation in both the neuroforamina—the spaces around the spine through which [nerve roots](#) pass into the [spinal cord](#)—and within the spinal cord itself. Study participants—including 16 patients with chronic radiculopathy and 10 control volunteers—had combined MR/PET imaging with a radiopharmaceutical that binds to TSPO, a marker for neuroinflammation. MR/PET imaging focused on neuroforamina in the lumbar spine for all participants, and in a subset of 18—9 patients and 9 controls—images were also taken of the sections of the lower spinal cord that are connected to the nerve roots affected in sciatica.

Overall the study results indicated that, compared with those of control participants, TSPO levels in sciatica patients were higher in both the neuroforamina and the spinal cord. The sciatica-associated elevations were seen in nerve roots on the side of affected legs and in spinal cord segments known to process sensory signals from the legs. Among 9 patient participants who received steroid injections as part of their clinical care—2 before the scanning and 7 after—only 5 experienced significant relief from the procedure, and those 5 all had results indicating higher neuroforaminal TSPO levels.

"The fact that patients with stronger TSPO elevations in the nerve roots

benefited most from a local anti-inflammatory treatment makes sense," says Loggia. "For patients who didn't benefit from steroid injections, the source of pain and inflammation may be the spinal cord or, as shown in our previous paper, the brain itself."

Zhang adds, "If larger studies confirm that the efficacy of steroid injections correlates with nerve root inflammation, physicians will have a way to identify which patients are most likely to benefit from the procedure. Our results also suggest that directly treating neuroinflammation in the spinal cord may help patients who don't respond to [steroid injections](#). Finding a way to treat spinal neuroinflammation for those [patients](#) is a goal that we are actively pursuing."

More information: Daniel S. Albrecht et al, Neuroinflammation of the spinal cord and nerve roots in chronic radicular pain patients, *Pain* (2018). [DOI: 10.1097/j.pain.0000000000001171](https://doi.org/10.1097/j.pain.0000000000001171)

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