

## **"Massachusetts General Hospital Study finds nerve damage in previously mysterious chronic pain syndrome"**

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*Study finds nerve damage in previously mysterious chronic pain syndrome  
Reduction in small-fiber nerves may underlie complex regional pain  
syndrome-I (reflex sympathetic dystrophy)*

BOSTON – Researchers at Massachusetts General Hospital (MGH) have found the first evidence of a physical abnormality underlying the chronic pain condition called reflex sympathetic dystrophy or complex regional pain syndrome-I (CRPS-I). In the February issue of the journal *Pain*, they describe finding that skin affected by CRPS-I pain appears to have lost some small-fiber nerve endings, a change characteristic of other neuropathic pain syndromes.

“This sort of small-fiber degeneration has been found in every nerve pain condition ever studied, including postherpetic neuralgia and neuropathies associated with diabetes and HIV infection,” says Anne Louise Oaklander, MD, PhD, director of the MGH Nerve Injury Unit, who led the study. “The nerve damage in those conditions has been much more severe, which may be why it’s been so hard to detect CRPS-I-related nerve damage.”

Complex regional pain syndrome is the current name for a baffling condition first described in the 19th century in which some patients are left with severe chronic pain and other symptoms – swelling, excess sweating, change in skin color and temperature – after what may be a fairly minor injury. The fact that patients’ pain severity is out of proportion to the original injury is a hallmark of the syndrome, and has led many to doubt whether patients’ symptoms are caused by physical damage or by a psychological disorder. Pain not associated with a known nerve injury has been called CRPS-I, while symptoms following damage to a major nerve has been called CRPS-II.

Because small-fiber nerve endings transmit pain messages and control skin color and temperature and because damage to those fibers is associated with other painful disorders, the MGH research team hypothesized that those fibers might also be involved with CRPS-I. To investigate their theory they studied 18 CRPS-I patients and 7 control patients with similar chronic symptoms known to be caused by arthritis. Small skin biopsies were taken under anesthesia from the most painful area, from a

pain-free area on the same limb and from a corresponding unaffected area on the other side of the body.

The skin biopsies showed that, the density of small-fiber nerve endings in CRPS-I patients was reduced from 25 to 30 percent in the affected areas compared with unaffected areas. No nerve losses were seen in samples from the control participants, suggesting that the damage was specific to CRPS-I, not to pain in general. Tests of sensory function performed in the same areas found that a light touch or slight heat was more likely to be perceived as painful in the affected areas of CRPS-I patients than in the unaffected areas, also indicating abnormal neural function.

“The fact that CRPS-I now has an identified cause takes it out of the realm of so-called ‘psychosomatic illness.’ One of the great frustrations facing CRPS-I patients has been the lack of an explanation for their symptoms. Many people are skeptical of their motivations, and some physicians are reluctant to prescribe pain medications when the cause of pain is unknown,” says Oaklander. “Our results suggest that CRPS-I patients should be evaluated by neurologists who specialize in nerve injury and be treated with medications or procedures that have proven effective for other nerve-injury pain syndromes.” She adds that the next research steps should investigate why some people are left with CRPS after injuries that do not cause long-term problems for most patients, determine the best way of diagnosing the syndrome and evaluate potential treatments.

“Investigations that identify the causes of disease are only possible if patients are willing to come to the lab and allow researchers to study them,” she adds. “We are tremendously grateful to these CRPS patients, whose willingness to let us study them – despite their chronic pain – allowed us to make an important step in helping those who suffer from this condition.” Oaklander is an assistant professor of Anaesthesia and Neurology at Harvard Medical School.

The study was supported by grants from The Mayday Fund, the National Institute for Neurological Disorders and Stroke, and the American Federation for Aging Research. Coauthors are Julia Rissmiller, Lisa Gelman, Li Zheng, MD, PhD; Yuchiao Chang, PhD; and Ralph Gott, all of the MGH.

Massachusetts General Hospital, established in 1811, is the original and largest teaching hospital of Harvard Medical School. The MGH conducts the largest hospital-based research program in the United States, with an annual research budget of nearly \$500 million and major research centers in AIDS, cardiovascular research, cancer, cutaneous biology, medical imaging, neurodegenerative disorders, transplantation biology and

photomedicine. In 1994, MGH and Brigham and Women's Hospital joined to form Partners HealthCare System, an integrated health care delivery system comprising the two academic medical centers, specialty and community hospitals, a network of physician groups, and nonacute and home health services.