Treatment blocks pain without disrupting other functions

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A combination of two drugs can selectively block pain-sensing neurons in rats without impairing movement or other sensations such as touch, according to a new study by National Institutes of Health (NIH)-supported investigators. The finding suggests an improved way to treat pain from childbirth and surgical procedures. It may also lead to new treatments to help the millions of Americans who suffer from chronic pain.

The study used a combination of capsaicin — the substance that makes chili peppers hot — and a drug called QX-314. This combination exploits a characteristic unique to pain-sensing neurons, also called nociceptors, in order to block their activity without impairing signals from other cells. In contrast, most pain relievers used for surgical procedures block activity in all types of neurons. This can cause numbness, paralysis and other nervous system disturbances.

"The Holy Grail in pain science is to eliminate pathologic pain without impairing thinking, alertness, coordination, or other vital functions of the nervous system. This finding shows that a specific combination of two molecules can block only pain-related neurons. It holds the promise of major future breakthroughs for the millions of persons who suffer with disabling pain," says Story C. Landis, Ph.D., director of the National Institute of Neurological Disorders and Stroke (NINDS) at the NIH, which funds the investigators' research along with the National Institute of Dental and Craniofacial Research (NIDCR) and the National Institute of General Medical Sciences (NIGMS). NINDS and NIDCR are co-

chairs of the NIH Pain Consortium. The study appears in the October 4, 2007, issue of Nature.*

Lidocaine, the most commonly used local anesthetic, relieves pain by blocking electric currents in all nerve cells. Although it is a lidocaine derivative, QX-314 alone cannot get through cell membranes to block their electrical activity.

That's where capsaicin comes in. It opens large pores called TRPV1 channels — found only within the cell membrane of pain-sensing neurons. With these channels propped open by capsaicin, QX-314 can pass through and selectively block the cells' activity.

The research team, led by Clifford J. Woolf, M.D., Ph.D., of Massachusetts General Hospital and Harvard Medical School and Bruce Bean, Ph.D., at Harvard Medical School, tested the combination of capsaicin and QX-314 in neurons isolated in Petri dishes and found that it blocked pain-sensing neurons without affecting other nerve cells. They then injected the drugs into the paws of rats and found that the treated animals could tolerate much more heat than usual. They also injected the two drugs near the sciatic nerve that runs down the hind leg. The treated rats did not show any signs of pain, and five of the six animals continued to move and behave normally. This showed that the drugs could block pain without impairing motor neurons that control movement.

The drug combination took half an hour to fully block pain in the rats. However, once it began, the pain relief lasted for several hours.

Source: National Institute of Neurological Disorders and Stroke