MedicalXpress

Neuroscientists explain inner workings of critical pain pathway

February 15 2007

Whether they're fighting postoperative soreness or relieving chronic discomfort from conditions such as cancer, morphine and other opioids are powerful weapons against pain. Now, in research published online in *Nature Neuroscience*, Brown University scientists give one reason why these painkillers work so well.

The secret: They act on a special form of N-type calcium channel, the cellular gatekeepers that help control pain messages passed between nerve cells. By blocking these channels, pain signals are inhibited. These findings not only shed important light on how the body controls pain, they could be a boon to drug development.

"We've known that drugs such as morphine are highly effective at blocking calcium channels, but we've never known precisely why – until now," said Brown neuroscientist Diane Lipscombe, who led the research. "With this new understanding of how opioids work on calcium channels, drug companies could develop effective new painkillers."

Lipscombe, a professor in the Department of Neuroscience, is an expert in N-type calcium channels, critical players in the pain pathway. At the synapse – the point of connection between nerve cells – N-type channels control the release of neurotransmitters. These chemicals carry messages between nerve cells – messages that include sensations of pain. So if you block N-type channels, you can block pain.

But all of these channels shouldn't be closed, Lipscombe explained.

That's because some pain signals – "That stove is hot!" – are needed to survive. "You don't want to shut off all pain signals," she said. "You just want to dampen some of them down."

In 2004, Lipscombe and her colleagues discovered a unique form of the N-type channel in nociceptors, neurons that carry pain signals to the spinal cord. These are the channels that opioids act on. But what makes the channels in nociceptors so special?

In their new work, Lipscombe and her team uncover the answer. All N-type channels are made up of a string of about 2,400 amino acids. In nociceptor N-type channels, that string differs by a mere 14 amino acids, Lipscombe and her team learned. This small difference in molecular make-up makes these channels much more sensitive to the pain-blocking action of opioids.

"In nociceptor N-type channels, you get double-barreled inhibitory action," she explained.

Source: Brown University