MedicalXpress

Old memory traces in brain may trigger chronic pain

June 4 2007

Why do so many people continue to suffer from life-altering, chronic pain long after their injuries have actually healed?

The definitive answer -- and an effective treatment -- has long eluded scientists. Traditional analgesic drugs, such as aspirin and morphine derivatives, haven't worked very well.

A Northwestern University researcher has found a key source of chronic pain appears to be an old memory trace that essentially gets stuck in the prefrontal cortex, the site of emotion and learning. The brain seems to remember the injury as if it were fresh and can't forget it.

With new understanding of the pain source, Vania Apkarian, professor of physiology, and of anesthesiology, at Northwestern's Feinberg School of Medicine, has identified a drug that controls persistent nerve pain by targeting the part of the brain that experiences the emotional suffering of pain. The drug is D-Cycloserine, which has been used to treat phobic behavior over the past decade.

In animal studies, D-Cycloserine appeared to significantly diminish the emotional suffering from pain as well as reduce the sensitivity of the formerly injured site. It also controlled nerve pain resulting from chemotherapy, noted Apkarian, who is a member of the Robert H. Lurie Comprehensive Cancer Center at Northwestern University.

The drug has long-term benefits. Animals appeared to be pain free 30

days after the last dose of a 30-day regime of D-Cycloserine.

The study, funded by the National Institutes of Health, will be published in the journal *Pain* this fall. (It has been published on-line.)

“In some ways, you can think of chronic pain as the inability to turn off the memory of the pain,” Apkarian said. “What’s exciting is that we now may be relieving what has clinically been the most difficult to treat—the suffering or the emotional component of pain.”

Scientists have always tried to understand pain from the viewpoint of sensation, Apkarian said. “To control it, they tried to stop the sensory input to the brain. ”We are saying there’s a cognitive memory and emotional component in the brain that seems abnormal. Easing that may have a bigger effect on suffering.”

Chronic pain is not caused by a single mechanism, Apkarian noted. Sensory abnormalities in people with chronic pain probably drive this memory abnormality.

About 10 percent of the United States population suffers from chronic pain, of which the majority is back pain.

One of Apkarian’s studies with rats tried to separately measure their emotional suffering and their physical pain after being treated with the drug. (The rats had chronic pain from a healed limb injury.) The results indicated the animals’ emotional suffering decreased much more than their physical pain. While the physical pain appeared to be reduced 30 percent – their emotional suffering completely disappeared.

Rat are nocturnal animals that prefer to be in the dark and are averse to bright light. Researchers placed the rats in a two-compartment chamber –- one side light, one dark. When the rats were in their preferred dark

side, scientists mechanically stimulated their sensitive limbs. The rats didn't like that and bolted into the bright chamber, where they remained. Next scientists took the same rats and treated them with D–Cycloserine. Again, scientists stimulated the rats' sensitive limbs. This time, however, the rats remained in the dark chamber.

"Their aversive reaction to the stimulation disappeared," Apkarian said.

Based on the animal results, the next step will be to test the drug in clinical trials, Apkarian said.

"When we do this in a clinical trial, we expect people to say I still have the pain, but it's not bothering me anymore," Apkarian said. "We think they will have a physical awareness of the pain, but its emotional consequences will have decreased." He said the drug potentially may lower the amount of standard analgesics people have to use.

In Apkarian's previous study, published in late 2006, he revealed that chronic back pain appears in a different part of the brain than the discomfort of burning your finger, for example. With a functional MRI, he found that chronic back pain shows up in the prefrontal cortex. By contrast, the acute sensory pain of the burned finger appears in the sensory part of the thalamus.

Apkarian also found that the longer a person has been suffering from chronic pain, the more activity in the prefrontal cortex. He was able to predict the years of their suffering from the MRI.

"It's cumulative memory," he explained. "I can predict with 90 percent accuracy how many years they have been living in that pain without even asking them the question."

Source: Northwestern University