Researchers turn pain perception on and off in mice using light

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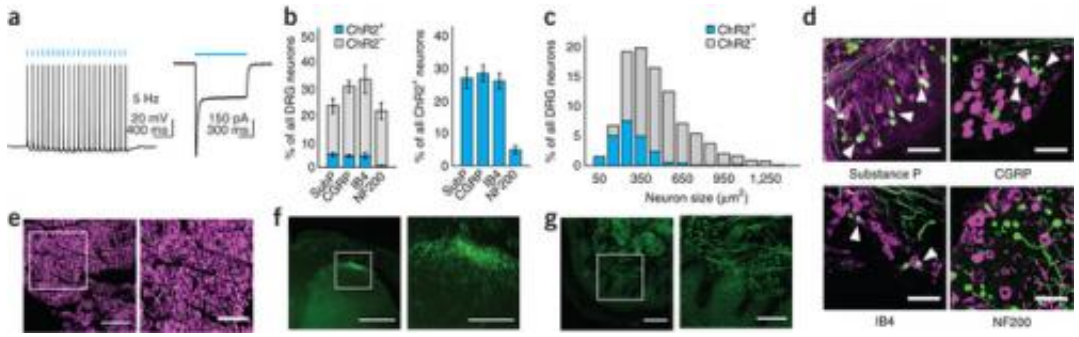

Intrasciatic injection of AAV6-hSyn-ChR2-eYFP results in transduction of unmyelinated nociceptors projecting to spinal cord lamina I/IIo. Credit: *Nature Biotechnology* (2014) doi:10.1038/nbt.2834

(Medical Xpress)—A team of researchers at Stanford University has found a way to turn the perception of pain on and off using only a light source. In their paper published in the journal *Nature Biotechnology,* the team describes how they genetically altered nerve receptors beneath the skin in mice, and how doing so allowed for controlling the perception of pain.

Optogenetics, the science of using a light source to control cell functions, was first pioneered a decade ago in a lab co-run by Karl Deisseroth. He's now one of the co-founders of Circuit Therapeutics, a San Francisco-based research lab. There, he and colleagues are working to find a ways to use optogenetics to ease the various forms of pain that people

experience. The idea is to genetically modify cells so that they respond in desired ways when light is shone on them. In this latest effort, the researchers did just that.

The team caused nerve cells just beneath the skin of several mice to respond to light—receptors were turned on or off—by first injecting a solution of molecules directly into the nerve endings. The skin on mice feet is so thin that light can pass right through it and on to the pain receptors below. Next, the team tested how well their solution worked by shining a light up at them through the floor of their cage. The mice flinched, cried out and licked their feet—all clear signs of pain. After that, the team attached tight bands to the paws of the treated mice, which normally causes pain, and then shone a different colored light onto them. This time, the treatment had the opposite effect—the mice appeared to be oblivious to the pain the bands were supposed to be causing. Thus, by shining two different colored lights on the impacted area, the researchers were able to turn pain perception on and off at will.

The researchers aren't suggesting that humans be injected with such chemicals any time soon. The whole point is to learn more about how light can be used to control cell activity and pain perception so that some new approach in the future can be used to help alleviate pain—the leading cause of doctor visits. The team notes that few good remedies now exist. Pills can help, but they can muddle the mind, cause constipation and lead to addiction. A simple hand-held flashlight device that allows a person to turn off pain at will would be a marked improvement.

More information: Virally mediated optogenetic excitation and inhibition of pain in freely moving nontransgenic mice, *Nature Biotechnology* (2014) DOI: 10.1038/nbt.2834

Abstract

Primary nociceptors are the first neurons involved in the complex processing system that regulates normal and pathological pain1. Because of constraints on pharmacological and electrical stimulation, noninvasive excitation and inhibition of these neurons in freely moving nontransgenic animals has not been possible. Here we use an optogenetic2 strategy to bidirectionally control nociceptors of nontransgenic mice. Intrasciatic nerve injection of adeno-associated viruses encoding an excitatory opsin enabled light-inducible stimulation of acute pain, place aversion and optogenetically mediated reductions in withdrawal thresholds to mechanical and thermal stimuli. In contrast, viral delivery of an inhibitory opsin enabled light-inducible inhibition of acute pain perception, and reversed mechanical allodynia and thermal hyperalgesia in a model of neuropathic pain. Light was delivered transdermally, allowing these behaviors to be induced in freely moving animals. This approach may have utility in basic and translational pain research, and enable rapid drug screening and testing of newly engineered opsins.