

New insights into the synaptic basis of chronic pain

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A team of scientists has found a novel road-block in the pain pathway, which could be used to treat chronic pain. Their results are published March 13 in the online, open-access journal *PLoS Biology*.

Pain is an important [physiological function](#) that protects our bodies from harm. Pain-sensing nerves transduce harmful stimuli into [electrical signals](#) and transmit this information to the brain via the spinal cord. However, when these nerves get activated persistently, such as after injury or inflammation, the information flow into the spinal cord is remarkably amplified. This phenomenon, termed 'synaptic long-term potentiation (LTP)', is an important biological property that is evolutionarily conserved from lower organisms to humans.

To gain a better understanding of how LTP works in the context of pain signaling, the team led by Rohini Kuner (Heidelberg University, Germany) and Ceng Luo (Fourth Military Medical University, China) took advantage of biochemical, genetic, physiological, and behavioral tools available in mice. They studied how LTP works at the synaptic connection between peripheral pain sensors and spinal cord neurons. They found that presynaptic events that unfold in the spinal endings of pain-sensing nerves are required for this pain amplification.

"Our results indicate that an enzyme termed cGMP-activated Kinase 1 (PKG-I) is a key player in this important process", says Ceng Luo. By removing PKG-1 specifically from the presynaptic neurons in this pathway, their group found that not only was LTP abolished, but that

pain-related memory and behavior were also altered. Can these basic biological findings be put to use? Chronic pain is a major cause of poor quality of life worldwide; recent [demographic studies](#) indicate that one in every six people in Europe suffers from chronic [pain](#).

"Our observation that genetically silencing PKG-I, or blocking its activation, in pain-sensing nerves markedly reduced chronic [inflammatory pain](#) paves the way for potential new therapeutic approaches," says Rohini Kuner.

More information: Luo C, Gangadharan V, Bali KK, Xie R-G, Agarwal N, et al. (2012) Presynaptically Localized Cyclic GMP-Dependent Protein Kinase 1 Is a Key Determinant of Spinal Synaptic Potentiation and Pain Hypersensitivity. *PLoS Biol* 10(3): e1001283. [doi:10.1371/journal.pbio.1001283](https://doi.org/10.1371/journal.pbio.1001283)

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