How the brain remembers pain

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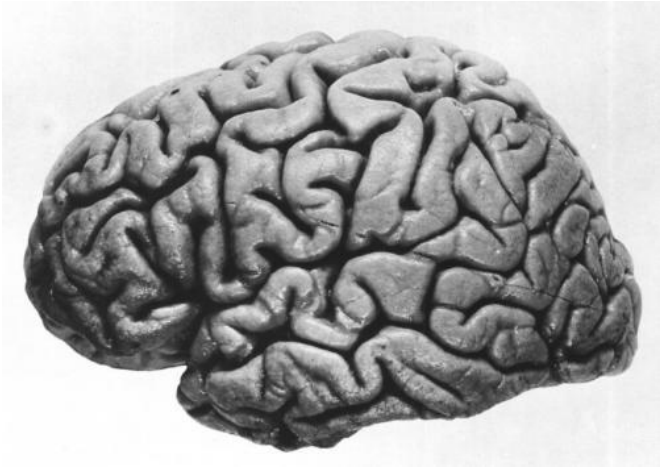

Left hemisphere of J. Pi?sudski's brain, lateral view. Credit: public domain

Scientists from Berne have discovered a mechanism, which is responsible for the chronification of pain in the brain. The results of their study suggest new strategies for the medical treatment of chronic pain.

Chronic pain is a common disease state, which affects more than one million people in Switzerland. Unfortunately, in a lot of cases proper treatment strategies are missing. "The constant perception of pain severely influences the quality of life of the patients and represents an extraordinary emotional burden", Thomas Nevian from the Department of Physiology at the University of Bern says. "Thus, understanding the development of chronic pain is of outmost importance for neuroscience research."

Together with fellow researcher Mirko Santello, Nevian has discovered a cellular mechanism in the brain of mice that contributes to the development of chronic pain. The findings of the two Bernese researchers resulted in the development of a novel pharmacological treatment strategy for chronic pain. The study was published in the scientific journal *Neuron*.

Traces of pain

Nevian and Santello investigated the modification of neurons by chronic pain in a brain region called Gyrus Cinguli, which is associated with the emotional aspects of pain. In this context the establishment of a "pain memory" plays an important role, as Thomas Nevian explains. "The neurons are constantly activated by a noxious stimulus, thus building a memory trace for pain that becomes irreversible. Our idea was to understand this mechanism better to derive potential new treatment strategies."

Pain is perceived by electrical impulses in the neurons. Therefore, the two researchers were searching for changes in the electrical properties of neurons in the limbic system. They found that neurons were more excitable in the Gyrus Cinguli. This was attributable to a down regulation of a specific ion channel, a protein in the cell membrane that determines the electrical properties of the cell. This led to an increased number of nerve impulses in these cells and thus to an increased perception of pain.

Serotonin receptors can alleviate pain

Santello and Nevian tried to manipulate this ion channel to reestablish its functionality. By activating a specific receptor sensitive to the neuromodulator serotonin they succeeded in reestablishing a normal function of the neuron. This reduced the pain perception in an animal model. "It has been known for some time that serotonin can modulate pain perception and the function of some drugs is based on this", Thomas Nevian says. "Nevertheless, what is new in our study now is that we were able to identify a specific subtype of serotonin receptor that reduced the perception of pain more efficiently. This is an important result, which might help to treat chronic pain more efficiently in the future."

Furthermore, the results of the study suggest a novel mechanism how established drugs of the tryciclic class of antidepressants work. So far it was assumed that these drugs act in the periphery on nociceptors and in the spinal cord. The two scientists demonstrated that these drugs can also act directly on the perception of pain in the brain. However, Thomas Nevian emphasizes that "even though we made an important step forward now, it will take some time before novel drugs will be designed based on our results".

More information: Santello M & Nevian T. "Dysfunction of cortical dendritic integration in neuropathic pain reversed by serotoninergic neuromodulation." *Neuron*, 2015 (in press) DOI: dx.doi.org/10.1016/j.neuron.2015.03.003

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