

## Chronic Pain – What is it?

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**Received date:** October 01, 2021; **Accepted date:** October 14, 2021; **Published date:** October 21, 2021.

**Citation:** James David Adams (2021), Chronic Pain – What is it?, J. New Medical Innovations and Research, 2(5): DOI: [10.31579/2767-7370/025](https://doi.org/10.31579/2767-7370/025)

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### Summary

The brain stem and brain are involved in chronic pain processing and sensation. This may involve changes in gene expression through epigenetic alterations [1]. Chronic pain is also a learned experience which involves the brain [2]. In chronic pain, thresholds to pain sensation decrease such that pain may be produced by nonpainful stimuli.

The body is endowed with a powerful pain sensing organ, the skin. The purpose of the skin is to rapidly sense and transmit pain signals in order to avoid damage to the body. Transient receptor potential cation channels on skin sensory neurons are responsible for rapidly transmitting pain signals [3]. There are several other skin receptors involved in pain sensation as well. The normal agonists for transient receptor potential cation channels are endocannabinoids. These channels become deactivated after a few minutes resulting in the disappearance of pain.

Trauma from a severe stimulus to a sensory neuron causes the release of chemokines [4] that attract macrophages and neutrophils into the skin. This establishes an inflammatory situation in the skin with the release of prostaglandins from macrophages and leukotrienes from neutrophils that activate transient receptor potential cation channels and other receptors to enhance and prolong pain [5]. Prostaglandins and interleukins released by macrophages induce the release of IL-17 by skin resident T cells, which enhances chemokine production [6]. Chemokines can also activate transient receptor potential cation channels. This establishes a pain chemokine cycle where pain releases chemokines that increase pain. The skin produces pain in chronic pain. This cycle can function for many years without subsiding. During pain, skin sensory neurons secrete inflammatory factors such as bradykinin, neurokinins, calcitonin gene-related peptide and other inflammatory proteins that enhance inflammation in susceptible areas [7].

Two cures for chronic pain have been reported, a liniment made from *Artemisia californica* and a foot bath made from *Salvia mellifera* [8-10]. The liniment has been shown to be superior to placebo [11]. Cure means the pain is gone and does not return. Several patients have been cured of chronic back pain, fibromyalgia and whip lash for several years already. These medicines come from Chumash Indian traditional medicine in California. They contain monoterpenoids that inhibit transient receptor potential cation channels in the skin [3], sesquiterpenoids that down regulate macrophage cyclooxygenase-2 [12] and diterpenoids that inhibit

IL-17 production [13]. These medicines are applied to the skin, function in the skin and evaporate from the skin with no need to penetrate into the blood. Several hundred patients have used these medicines with no reported toxicity.

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DOI: [10.31579/2767-7370/025](https://doi.org/10.31579/2767-7370/025)

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