

Chronic pain is a major medical problem. However, current analgesics are not effective in many types of chronic pain. A research team led by Dr. Chih-Cheng Chen, Institute of Biomedical Sciences, Academia Sinica has discovered a novel antinociceptive mechanism against acid-induced chronic muscle pain. This finding is essentially opposite to the role that substance P (SP) has been proposed to play over many years—SP signaling promotes pain. This finding is published in a recent paper in Proceedings of the National Academy of Sciences (PNAS) and is highlighted in a front section of the printed journal.

SP is an undecapeptide belonging to the tachykinin small peptide family. SP is an excitatory neurotransmitter that helps to excite and transmit pain signals. SP signaling is almost excitatory in almost all neuronal cells, including neurons in spinal dorsal horn, brain stem, hippocampus, and dorsal root ganglia, etc. Substances that inhibit SP signaling pathways generally show antinociceptive effects in animal models. However, though high levels of SP in muscle tissues and spinal fluid are frequently associated with chronic muscle pain, such as myofascial pain syndrome and fibromyalgia, researchers do not fully understand the role of SP in muscle pain.

The IBMS research team has used mouse models to test how SP contributes to muscle pain sensitivity. The researchers found that in contrast to SP's usually excitatory role, mice lacking SP signaling showed increased pain sensitivity after intramuscular acid injections, compared with mice with normal SP signaling. Both mice with null mutation of SP gene and those administrated with SP receptor antagonists showed similar increased sensitivity to muscle pain. Further electrophysiological studies on muscle nociceptors showed that the SP signaling mediated an M-type potassium channel opening to inhibit the neural excitation. This inhibitory effect of SP is exclusively found in muscle nociceptors that express acid-sensing ion channel 3.

This study opens up a new direction for pain research and also partially annotates the failure of clinical trials for analgesic drugs based on SP antagonism. The research team is now working on analgesic drug development against chronic muscle pain.

The full article entitled "[An Antinociceptive Role for Substance P in Acid-induced Chronic Muscle Pain](#)"

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