The Antinociceptive Mechanisms of Low-Frequency Electroacupuncture in Inflammatory Pain Model

Chun-Ping Huang[1], Hong-Lin Su[1], and Yi-Wen Lin[2,*]

[1]*Department of Life Sciences, National Chung Hsing University, Taichung 402, Taiwan, R.O.C.*
[2]*Graduate Institute of Acupuncture Science, China Medical University, Taichung 40402, Taiwan, R.O.C.*

Pain is associated with conditions such as inflammation, trauma, diabetes, arthritis or tumor, which can result from altered properties of peripheral nerves. As a result, this leads to increased spontaneous firing or alterations in their conduction properties. Nociception comprises the processes of transduction, conduction, transmission, and perception. Voltage-gated sodium channels (Na_vs) control the influx of Na^+ ions into the neurons and play an essential role in the initiation and propagation of nociception action potentials in dorsal root ganglion (DRG) neurons. PKA and PKC phosphorylate $Na_v1.8$ and increase TTX-resistant Na^+ currents. Acupuncture is known to stimulate the Aδ-fibers and modulate pain sensation by activating C-fibers through the meridian. Several studies have suggested that acupuncture increases the release of endogenous opioids, serotonin, and adenosine to reduce pain. We first established inflammatory pain animal model by injection of CFA in the mice plantar surface of the hind paw. Behavior tests were conducted at day 4 after induction of inflammation, and DRGs were harvested after behavior tests. Low-frequency 2-Hz electroacupuncture (LFEA) at Zusanli (ST36) acupoint reliably attenuated CFA-induced mechanical and thermal hyperalgesia (by von Frey, radial heat test). The phenomenon was not observed in sham group. Inflammation increased the expression of $Na_v1.8$ and LFEA-elicited down-regulation of $Na_v1.8$. To investigate analgesia mechanism by LFEA, we further injected CPA, adenosine A1 receptor (A1AR) agonist (0.1 mg/kg), at ST36 acupoint or endomorphin 1, μ-receptor (MOR) agonist (10 mg/kg) intraperitoneally. The results show LFEA, could improve animal pain behaviors and down-regulate the expression of COX-2 and phosphorylated PKCε.

Key words: Electroacupuncture, analgesia, voltage-gated sodium channels