Wound-healing growth factor, basic FGF, induces Erk1/2-dependent mechanical hyperalgesia

Abstract:
Growth factors such as nerve growth factor and glial cell line-derived neurotrophic factor are known to induce pain sensitization. However, a plethora of other growth factors is released during inflammation and tissue regeneration, and many of them are essential for wound healing. Which wound-healing factors also alter the sensitivity of nociceptive neurons is not well known. We studied the wound-healing factor, basic fibroblast growth factor (bFGF), for its role in pain sensitization. Reverse transcription polymerase chain reaction showed that the receptor of bFGF, FGFR1, is expressed in lumbar rat dorsal root ganglia (DRG). We demonstrated presence of FGFR1 protein in DRG neurons by a recently introduced quantitative automated immunofluorescent microscopic technique. FGFR1 was expressed in all lumbar DRG neurons as quantified by mixture modeling. Corroborating the mRNA and protein expression data, bFGF induced Erk1/2 phosphorylation in nociceptive neurons, which could be blocked by inhibition of FGF receptors. Furthermore, bFGF activated Erk1/2 in a dose- and time-dependent manner. Using single-cell electrophysiological recordings, we found that bFGF treatment of DRG neurons increased the current-density of NaV1.8 channels. Erk1/2 inhibitors abrogated this increase. Importantly, intradermal injection of bFGF in rats induced Erk1/2-dependent...
mechanical hyperalgesia. Perspective: Analyzing intracellular signaling dynamics in nociceptive neurons has proven to be a powerful approach to identify novel modulators of pain. In addition to describing a new sensitizing factor, our findings indicate the potential to investigate wound-healing factors for their role in nociception.

Stichworte: Pain Nociception Peripheral Sensory Neuron Sensitization Signaling Inflammatory Pain Wound Healing Quantitative Automated Microscopy Bfgf Fgf-2 Fgf-beta Map Kinase Erk1/2 Na(v)1.8 Voltage Gated Sodium Channels Randall Selitto

Zeitschriftentitel: Pain
Jahr: 2013
Band: 154
Heft / Issue: 10
Seiten: 2216-2226

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Mathematik > Zentrum Mathematik > M12 Mathematische Modelle biol. Systeme (Prof. Theis) > Lehrstuhl für Mathematische Modelle biol. Systeme (Prof. Theis)