Reduced excitability of gp130-deficient nociceptors is associated with increased voltage-gated potassium currents and Kcna4 channel upregulation.

Neuropathic pain and pain arising from local inflammation are characterized by increased release of inflammatory mediators like interleukin-6 (IL-6) by immune cells. The levels of IL-6 is increased in various painful conditions and correlates with the severity of thermal and mechanical hypersensitivity. Deletion of the IL-6 signal transducer glycoprotein 130 (gp130) reduces inflammation associated with hypersensitivity to thermal and mechanical stimuli. In this study, we show that nociceptor-specific deletion of gp130 alters excitability parameters that are linked to changes in the potassium conductance. In SNS-gp130(-/-) sensory neurons, the resting membrane potential was reduced. Moreover the repolarization speed of the action potential and afterhypolarization was augmented, however, voltage-gated Na(+) and Ca(2+) current were not obviously altered. The main difference between gp130-deficient and control neurons was a significant increase in the conductance of both delayed rectifier as well as A-type potassium currents. Taqman RT-PCR analysis revealed significantly higher levels of Kcna4 mRNA, encoding A-type Kv1.4 potassium channel, in neuron cultures from SNS-gp130(-/-) versus control mice, which may account for the electrophysiological data. No difference in other voltage-gated ion channel mRNAs was observed. The
present data show for the first time increased A-type K(+) currents and expression of voltage-gated potassium channel Kcna4 (Kv1.4) in SNS-gp130(-/-) nociceptors. This suggests that gp130 acts as a break for the expression of potassium channels and important regulator hub for nociceptor excitability.