

**Abstract**

Neuropathic pain is a chronic debilitating disease that results from nerve damage, possibly after the injury has healed, and is characterized by spontaneous pain and mechanical hyperalgesia. Although loss of inhibitory tone in the dorsal horn of the spinal cord is a major contributor to neuropathic pain, the molecular and cellular mechanisms underlying these dysfunctions are unclear. Here, we combined pharmacogenetic activation and selective ablation approaches in mice to define the contribution of spinal cord parvalbumin (PV) expressing inhibitory interneurons on native and neuropathic pain conditions. Ablating PV neurons in mice with nerve injury alleviates mechanical hyperalgesia. These findings indicate that PV interneurons are modulatory-specific filters that gate mechanical but not thermal inputs to the dorsal horn and that increasing PV interneuron activity can ameliorate the mechanical hyperalgesia that develops following nerve injury.

**Methods**

**Mouse strains**

PV-Cre, GFP and Elav2 reporter mice were obtained from Jackson Labs (stock numbers 002909, 007694 and 000974, respectively). TRPV1-cre mice were made by A.I.B. All experiments were performed on male 8-14 week-old mice, according to the Guidelines of the Animal Care Committee of McGill University.

**Primary antibodies**

were used in 1% NGS (in the indicated concentration): PKCγ (rabbit, 1:2,000; Sigma), GAD67 (mouse, 1:2,000), GAD65 (rabbit, 1:2,000), GABA (rabbit, 1:2,000), Signal挂钩 (1:500) provided by A. Kamitani, Gephyrin (mouse, 1:500), Synaptophysin (1:4517151), OX-172 (rabbit, 1:200), Synaptophysin (1:272001) and 3-Tubulin (rabbit, 1:20,000; Santa Cruz #C-19), FOS (rabbit, 1:2,000; Sigma), AVP (rabbit, 1:1000; AVES #GFP-1020 and #TUJ), GABA (rabbit, 1:2,000; Sigma), connexin 43 (rabbit, 1:200; Abcam), CaMKII (rabbit, 1:500; Millipore 05-737), PKCγ (rabbit, 1:2,000; Sigma-Aldrich #2540), Neuropathic pain condition, we used two different models: the spared nerve injury (SNI) model, and the intraplantar injection of capsaicin, which develops following nerve injury.

**Nature of PV neurons of LIII**

PV-Cre, M3DFlmato transgenic mice receptacle endogenous PV expression.

**Saporin virus strategy**

**Detachment of PV neuron processes in neuropathic pain**

**Specific ablation of PV neurons**

**Conclusion**

Pain injury: PAIN

Nerve injury: Allodynia

To Brain

**LIII PV neuron processes**

**Glycnergic inhibition of PKCy neurons**

**PV processes contact PKCy neurons**

**Modulation of PV neuron activity during sensory processing**

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