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Presentation Abstract

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Presentation Title: Nerve growth factor-triggered nociceptor sprouting induces mirror-image pain

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Abstract: Mirror-image pain, the mechanical hypersensitivity in the contralateral uninjured side, is a part of Complex Regional Pain Syndrome of poorly understood pathological mechanism. Kv4.3 is normally expressed in the cell bodies of a subset of mechanosensitive nociceptors in the dorsal root ganglion (DRG). Here, using unilateral ligation of rat lumbar(L) 5 and 6 spinal nerves to evoke mirror-image pain, we found significant changes in the contralateral DRGs instead of dorsal spinal cord, including activation of satellite glia, a rise of nerve growth factor (NGF), dendrite-like neurites sprouting from Kv4.3-expressing nociceptors, and axon-like neurites sprouting from other nociceptors. The rise of NGF was abolished when satellite glia were inhibited. Intrathecal injection of NGF into naïve rats induced bilateral nociceptor sprouting and mechanical hypersensitivity. Early anti-NGF therapy effectively reversed ligation-induced nociceptor sprouting and mirror-image pain but not satellite glia activation. In vitro studies showed that anti-NGF could reverse nociceptor sprouting during neurite outgrowth but had no effect in fully extended neurites. One step further, electrophysiological recording revealed that NGF-evoked nociceptor excitability was required for NGF-triggered nociceptor sprouting. These results indicate that an extra amount of

NGF released from satellite glia in the contralateral DRGs is sufficient to trigger nociceptor sprouting after unilateral nerve injury. Based on the robust induction of pre- and post-synaptic proteins in sprouted neurites, it is likely that a structural reorganization of pain signaling circuitry in the contralateral DRGs maintains mirror-image pain into a chronic state.

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dorsal root ganglion

neurite sprouting

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