SENSORY SYSTEMS

A touch of regulation

CORBIS

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Different types of mechanical stimuli activate different types of mechanosensory neurons to convey the sensation of touch or pain. Opioids are well-known regulators of pain, but a new study provides evidence that these molecules, acting mainly via δ-opioid receptors (DORs), can also regulate touch.

The cell bodies of many cutaneous mechanosensory neurons reside in the dorsal root ganglion (DRG). The authors previously showed in DOR–green fluorescent protein (DORGFP) knock-in mice that most DORGFP-expressing (DORGFP$^+$) DRG neurons have large-diameter cell bodies and express neurofilament heavy chain (NFH). Here, they found that *Oprd1* mRNA, which encodes DOR, was concentrated in wild-type NFH$^+$ large-diameter DRG neurons, and that the pattern of DOR radioligand binding in the wild-type mouse CNS was similar to the DORGFP expression pattern in knock-in mice, suggesting that DORGFP expression mimics native DOR expression.

The authors found that many DORGFP$^+$ NFH$^+$ DRG neurons expressed the neurotrophin receptors TRKC and RET, an expression profile consistent with that of touch-sensitive cutaneous mechanoreceptors. Moreover, they found that DORGFP$^+$ NFH$^+$ axons innervated Merkel cells and Meissner corpuscles, which are mechanosensory skin structures that are innervated by Aβ low-threshold mechanoreceptors, which respond to light touch. Together, these data suggest that many DOR$^+$ DRG neurons correspond to neurons that are touch-sensitive.

The authors also identified DORGFP$^+$ NFH$^+$ DRG fibres around hair follicles in the skin and as cutaneous free nerve endings, and mechanical stimulation of such fibres elicited responses in all cases. About half of the analysed neurons exhibited conduction velocities that resembled those of Aδ nociceptors, suggesting that these neurons are in fact Aδ mechanonociceptors. However, another population of these neurons exhibited conduction velocities that were in line with low-threshold mechanoreceptors. Thus, DORs are expressed in neurons that respond to innocuous mechanical stimuli.

DORGFP$^+$ NFH$^+$ DRG neurons send projections to the spinal cord as well as to the skin. In spinal cord slices, the authors found that deltorphin II — a selective DOR agonist — reduced the peak amplitude of excitatory postsynaptic currents in spinal neurons following application of a stimulus to the dorsal root that is known to induce glutamate release from Aβ fibres. This effect could be mimicked by inactivating the G proteins coupled to DORs, suggesting that activation of presynaptic DORs inhibits glutamate release from myelinated mechanoreceptors.

Together, these data indicate that DORs are broad regulators of mechanosensation, and that selective targeting of these receptors in myelinated mechanosensory neurons might be a viable strategy for treating nerve injury-induced mechanical hypersensitivity.

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ORIGINAL RESEARCH PAPER Bardoni, R. *et al.* Delta opioid receptors presynaptically regulate cutaneous mechanosensory neuron input to the spinal cord dorsal horn. *Neuron* http://dx.doi.org/10.1016/j.neuron.2014.01.044 (2014)