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PAIN

GDNF: the vital clue for pain relief?

The neuropathic pain that follows damage to peripheral nerves is often intense and persistent, and is largely refractory to traditional analgesia. The aetiology of neuropathic pain is something of a mystery, although there is evidence for a host of changes following the type of nerve damage that precipitates neuropathic pain. These include changes to the putative neurotransmitter/modulator systems, receptors and ion channels of sensory neurons.

Glial cell line-derived neurotrophic factor (GDNF) promotes survival of some sensory axons during development and has a neuroprotective effect on damaged sensory neurons in adults. The application of GDNF could therefore be a potential therapeutic strategy for the treatment of neuropathic pain. A recent report in *Science* gives an important boost for this approach by providing strong evidence that infusion of GDNF may prevent and even reverse the sensory abnormalities that develop in animal models of neuropathic pain.

Boucher and colleagues continuously infused GDNF into the spinal cord of adult rats in two models of neuropathic pain (partial ligation of one sciatic nerve, or ligation of the fifth lumbar nerve). The pronounced mechanical and thermal hyperalgesia that developed within a couple of days of ligation and persisted for the two-week observation period was blocked by GDNF infusion. Importantly, this blockade occurred even when the infusion began two days after ligation, when



neuropathic pain behaviour was established.

This finding was extended by a series of experiments that focused on the mechanism of this effect. Animal models indicate that the generation of neuropathic pain depends critically on the development of spontaneous ectopic activity in damaged neurons. Boucher and colleagues showed that the ectopic firing induced by ligation was reduced by GDNF, possibly through

the reversal of voltage-gated sodium channel plasticity induced by injury. This study therefore provides a rationale for GDNF treatment in neuropathic pain.

Peter Collins

References and links

ORIGINAL RESEARCH PAPER Boucher, T. J. *et al.* Potent analgesic effects of GDNF in neuropathic pain states. *Science* **290**, 124–127 (2000)

ENCYCLOPEDIA OF LIFE SCIENCES Pain and analgesia

FURTHER READING Trophic support

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