Cytokine modulation is necessary for efficacious treatment of experimental neuropathic pain

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Neuropathic pain originates from a damage or disease affecting the somatosensory system. Its treatment is unsatisfactory as it appears refractory to most analgesics. Animal models of neuropathic pain are now available that help to clarify the underlying mechanisms. Recently it has been recognized that inflammatory and immune mechanisms in the peripheral and in the central nervous system play a role in the onset and the maintenance of pain. In response to nervous tissue damage, activation of resident or recruited immune cells leads to the production of inflammatory mediators, as cytokines. In models of neuropathic pain, such as nerve injury and diabetes induced neuropathy, we have characterized the time course of the expression of the proinflammatory cytokines TNF-alpha, IL-1beta and IL-6 and of the antiinflammatory cytokine IL-10 both in the peripheral (sciatic nerve, dorsal root ganglia) and the central (spinal cord) nervous system. These cytokines appear activated/modulated in the nervous tissue in parallel with the occurrence of painful behaviour, i.e. allodynia and hyperalgesia. Novel therapeutic approaches efficacious to reduce painful symptoms, for example treatments with the non specific purinergic antagonist PPADS, and a cell stem therapy with stem cells of different origin (murine neuronal stem cells or human mesenchymal stromal cells from adipose tissue), also re-established a balance between pro and antinflammatory mediators in the peripheral and central nervous system. These data suggest a pivotal role of immune system and inflammation in neuropathic pain. The modulation of cytokines appears to be a common trait accomplished throughout different mechanisms by different treatments that might converge in neuropathic pain modulation.