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Importance of glial activation in neuropathic pain.

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Abstract

Glia plays a crucial role in the maintenance of neuronal homeostasis in the central nervous system. The microglial production of immune factors is believed to play an important role in nociceptive transmission. Pain may now be considered a neuro-immune disorder, since it is known that the activation of immune and immune-like glial cells in the dorsal root ganglia and spinal cord results in the release of both pro- and anti-inflammatory cytokines, as well as algesic and analgesic mediators. In this review we presented an important role of cytokines (IL-1alfa, IL-1beta, IL-2, IL-4, IL-6, IL-10, IL-15, IL-18, TNFalpha, IFNgamma, TGF-beta 1, fractalkine and CCL2); complement components (C1q, C3, C5); metaloproteinases (MMP-2,-9) and many other factors, which become activated on spinal cord and DRG level under neuropathic pain. We discussed the role of the immune system in modulating chronic pain. At present, unsatisfactory treatment of neuropathic pain will seek alternative targets for new drugs and it is possible that anti-inflammatory factors like IL-10, IL-4, IL-1alpha, TGF-beta 1 would fulfill this role. Another novel approach for controlling neuropathic pain can be pharmacological attenuation of glial and immune cell activation. It has been found that propentofylline, pentoxifylline, minocycline and fluorocitrate suppress the development of neuropathic pain. The other way of pain control can be the decrease of pro-nociceptive agents like transcription factor synthesis (NF-kappaB, AP-1); kinase synthesis (MEK, p38MAPK, JNK) and protease activation (cathepsin S, MMP9, MMP2). Additionally, since it is known that the opioid-induced glial activation opposes opioid analgesia, some glial inhibitors, which are safe and clinically well tolerated, are proposed as potential useful ko-analgesic agents for opioid treatment of neuropathic pain. This review pointed to some important mechanisms underlying the development of neuropathic pain, which led to identify some possible new approaches to the treatment of neuropathic pain, based on the more comprehensive knowledge of the interaction between the nervous system and glial and immune cells.

KEYWORDS: Astroglia; Glial inhibitors; Microglia; Neuropathic pain; Opioids

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