

## ***The Role of central neuroimmune activation in neuropathic pain and opioid Tolerance/Hyperalgesia***

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### ***Abstract***

Common cellular and molecular mechanisms are not only involved in the development of neuropathic pain caused by neurological damage but also in the occurrence of the tolerance/hyperalgesia phenomenon caused by chronic use of opioids. It seems that the activation of the neuroimmune system in the brain and spinal cord is one of the most important mechanisms involved in the initiation and maintenance of neuropathic pains and reducing the antinociceptive effect of morphine after nerve injury. Plus, it also plays an important role in the development of tolerance/hyperalgesia due to chronic opioid consumption. Glial cells, especially microglia, are resident immune cells in the nervous system and get activated in response to many exogenous and endogenous factors. When activated, glial cells undergo structural and functional changes and can secrete various inflammatory factors such as IL1 $\beta$ , IL6 and TNF $\alpha$ . These changes increase the irritability and spontaneous firing of neurons, which play an important role in creating and maintaining neuropathic pain as well as reducing the analgesic effect of opioids and bringing about the onset of opioid tolerance/hyperalgesia phenomenon. In this review, we have tried to observe recent studies on the role of the neuroimmune system of the brain and spinal cord in the development of neuropathic pain and of opioid tolerance/hyperalgesia. In our view, a prevention of activation or a diminished activity of the neuroimmune system via appropriate drug compounds can be useful as a new strategy in the treatment of neuropathic pain and in the decrease of morphine tolerance/hyperalgesia, which will in turn result in an increase of the clinical efficacy of opioids.

**Keywords:** Neuropathic pain; Hyperalgesia; Glia; morphine tolerance/hyperalgesia; opioids