CS03-01

LEARNING AND MEMORY IN PAIN PATHWAYS

J. Sandkühler
Center for Brain Research, Medical Universitiy of Vienna, Vienna, Austria

Hyperalgesia frequently results from injuries or inflammation of peripheral tissues, including nervous tissue and paradoxically also from the treatment with μ-opioid receptor agonists. Compelling evidence indicates that signal amplification in central pain pathways plays an important role for the maintenance of hyperalgesia[1]. In superficial spinal dorsal horn synaptic transmission between nociceptive C-fibres and lamina I projection neurons can be potentiated for prolonged periods of time in an activity dependent manner. These forms of synaptic long-term potentiation (LTP) can be securely prevented when opioids are applied during afferent stimulation. The blockage of LTP induction by opioids is a likely mechanism or pre-emptive analgesia. Upon withdrawal from high doses of opioids, however, LTP may develop at C-fibre synapses. During the latter form of LTP induction presynaptic activity at C-fibres is depressed rather than enhanced. Despite these fundamental differences in the induction, activity dependent- and opioidergic LTP share signalling pathways. This includes the activation of NMDA receptors, the rise in postsynaptic Ca^{2+} concentration and the activation of protein kinase C. Induction of opioidergic LTP further requires postsynaptic G-protein coupling which is in contrast to the presynaptic inhibition by opioids. LTP induction is abolished by blocking the Ca^{2+} rise upon withdrawal from the opioids. It is likely that the potentiation in synaptic strength translates into enhanced pain behaviour[1]. Plasticity at the first synapse in pain pathways is a promising target for the prevention and treatment of hyperalgesia of various origins.

Sandkühler J, Models and Mechanisms of Hyperalgesia and Allodynia. Physiological Reviews 89 (2009) 707-758.

https://doi.org/10.1016/S0924-9338(11)73478-2 Published online by Cambridge University Press