Palmitoylethanolamide restores pain and cognitive impairments and improves theta-burst long-term potentiation (LTP) in the dentate gyrus of neuropathic mice.

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Chronic pain is a devastating consequence of injury to the CNS or peripheral nervous system that results in the enhanced transmission of pain messages, thus representing a debilitating condition with a strong impact on the quality of life. Consequently, noxious stimuli are perceived as amplified painful sensation (hyperalgesia), whereas normal, harmless stimuli are painful (allodynia). Neuropathic pain could be enrolled in the group of neurological and psychiatric conditions, indeed patients with chronic pain exhibit increased anxiety, depression, and deficits in learning and memory (Guida et al., 2015). The hippocampal formation is an integral part of the Papez circuit involved in learning, memory, emotion, and motivation. Long-term potentiation (LTP) in the hippocampus has received attention as the biological basis for learning and memory. The activation of cannabinoid receptors, either directly by natural or synthetic agonists, or indirectly by selective inhibitors of the inactivation of endogenous cannabinoid receptor ligands (endocannabinoids), is widely supported by recent studies for neuropathic pain management. In this study, the impact of chronic pain condition on the hippocampal synaptic plasticity and on the related behavioral responses, has been investigated, in a murine model of spared nerve injury (SNI), 30 days post-surgery (Decostered and Woolf, 2000). Moreover, we studied the effect of chronic treatment with N- palmitoylethanolamide (PEA), an endogenous fatty acid amide, that exerts a great variety of biological functions associated to chronic pain and inflammation.

Our results showed, in 30 days SNI mice, a reduction of alternation in the Y-maze task, of recognition index in the Novel Object Recognition (NOR) test and of open-arm choice in the elevated plus-maze test but it induced an increase of the time of immobility in the tail suspension test, as compared to the control group (Sham mice). Furthermore the neuropathic mice presented an impairment of LTP in the granule cells of dentate gyrus induced by theta-burst stimulations (TBS) of the perforant path (PP) in the entorhinal cortex (Jedlicka et al., 2009). In fact when the entorhinal cortex was electrically stimulated, a great potentiation of the EPSP (LTP), was observed in the ipsilateral hippocampus, in Sham mice.

PEA chronic treatment (14 days) increased the alternation in the Y-maze task and the recognition index in the NOR test and decreased the immobility time in the tail suspension test, suggesting that PEA was able to improve memory deficits and the depressive-like behavior but not the anxiety-like behavior associated to neuropathic pain. Finally, PEA partially restored the LTP in the dentate gyrus in 30 days SNI mice.

Overall, these results suggest that neuropathic pain negatively affect the limbic and cognitive functions, which may underlie the deficiency of LTP, and the possible use of natural compounds such as PEA for the treatment of neuropathic pain.

References:

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