Effects of palmitoylethanolamide on release of mast cell peptidases and neurotrophic factors in a murine model of spinal cord injury

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Spinal cord injury (SCI) has a significant impact on quality of life, expectancy, and economic burden, with considerable costs associated with primary care and loss of income. The complex pathophysiology of spinal cord injury (SCI) may explain the difficulty in finding a suitable therapy for limiting neuronal injury and promoting regeneration. Although innovative medical care, advances in pharmacotherapy have been limited. The aim of the present study was to carefully investigate molecular pathways and subtypes of glial cells involved in the protective effect of PEA on inflammatory reaction associated with an experimental model of SCI. A number of experimental animal models have been developed to simulate the pathophysiology of acute clinical spinal cord injury in humans. The compression model induced by applying an aneurysm clip to the spinal cord is closer to the human situation, since it replicates the persistence of cord compression. Spinal cord trauma was induced in mice by the application of vascular clips (force of 24 g) to the dura via a four-level T5-T8 laminectomy. Repeated PEA administration (10 mg/kg ip., 6 and 12 h after SCI) significantly reduced the degree of the severity of spinal cord trauma through the reduction of mast cell infiltration and activation (evaluated as tryptase and chymase expression). Moreover, PEA treatment significantly reduced astrogliosis, and the increased cannabinoid CB_2 receptor expression in microglia after SCI. Importantly, the protective effect of PEA involved changes in the expression of neurotrophic factors, and in spinal cord dopaminergic function.

Our results enhance our understanding about mechanisms related to the anti-inflammatory property of the PEA suggesting that this N-acylethanolamines may represent a crucial therapeutic intervention both diminishing the immune/inflammatory response and promoting the initiation of neurotrophic substance after SCI.