Palmitoylethanolamide chronic treatment reduces the sensorial and cognitive disfunctions associated with mild traumatic brain injury

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Traumatic brain injury (TBI) represents a major public health problem. Traumatic brain injury (TBI) initiates a neuroinflammatory cascade that contributes to neuronal damage and behavioral impairment. Cannabinoids of all classes have the ability to protect neurons from a variety of insults that are believed to underlie delayed neuronal death after traumatic brain injury (TBI), including excitotoxicity and neuroinflammation.

We investigated the anti-neuroinflammatory properties of the palmitoylethanolamide (PEA), a commercially available compound with a pleiotropic mechanism of action.

We applied a model of mild TBI that develop sensorial and cognitive disfunctions. In particular, mice developed abnormal pain sensation (allodynia) and depression associated to repetitive, obsessive-compulsive behaviours. According to the literature, we found that TBI increased the number of proinflammatory/hypertrophic microglial cells in specific areas of the brain. We observed that PEA chronic treatment (10 mg/kg i.p.), significantly ameliorate the mechanical allodynia associated with TBI. Moreover, cognitive impairment associated with TBI such as depression and aggressiveness were reduced by PEA treatment. In particular, we measured the immobility time in sham, TBI and TBI treated animals in the tail suspension test and the results revealed that, while TBI animals showed an increased immobility time, PEA chronic treatment determined a reduction of depressive-like behaviour. Finally, we found that PEA, through a genomic mechanism PPAR-α-mediated, increased the expression level of CB2 cannabinoid receptor in primary microglial cells and, hence, could be responsible of the phenotype switch from pro to an anti-inflammatory/neuroprotective microglia.

Our results show a possible use of natural compounds such as PEA together with the already used drugs for the treatment of severe brain injury. Moreover, the discovery of new mechanisms in endogenous lipid compound could represent a new pharmacological tool to develop new molecules for the treatment of chronic neurological disorders