

# Palmitoylethanolamide reduces formalin-induced neuropathic-like behaviour through spinal glial/microglial phenotypical changes in mice

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Palmitoylethanolamide (PEA) is an endogenous cannabinoid-like compound in the central nervous system, which can modulate several functions in different pathological states, such as inflammation and pain response (1,2). We have here investigated the effect of PEA (5-10 mg/kg) on mechanical allodynia and thermal hyperalgesia 3 and 7 days following peripheral injection of formalin. Moreover, we investigated PEA effect on the glial/microglial phenotypical changes associated with spinal neuronal sensitization. Formalin induced a significant decrease of thermal and mechanical withdrawal threshold in the injected and contralateral paw. PEA chronic treatment (once per day) significantly reduced mechanical allodynia and thermal hyperalgesia in a dose-dependent manner. Consistently, *in vivo* electrophysiological recordings revealed a significant increase of the duration and frequency, and a rapid decrease in the onset of evoked activity of the spinal nociceptive neurons 7 days after formalin. PEA normalized the electrophysiological parameters in a dose-dependent manner. We found that formalin induced a significant microglia and glia activation normalized by PEA, together with increased expression of glial interleukin 10. In conclusion these data confirm the potent anti-inflammatory and anti-allodynic effect of PEA, which possibly acts on microglial/glial cells at spinal cord level.

## References

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