

## **Title: Effects of palmitoylethanolamide in cocaine-induced behaviours**

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**Aims.** Cocaine addiction is a chronically relapsing disorder characterized by the compulsion to seek and take the drug. Previous investigations have demonstrated that several drugs of abuse, as cocaine, can alter the levels of lipid-based signalling molecules such as the N-acylethanolamines (NAEs). In addition, NAEs levels in the brain are sensitive to cocaine self-administration and extinction training. In this context, this study aimed to investigate the effect of repeated and acute palmitoylethanolamide (PEA), an endogenous NAE, on the behavioural effects of cocaine using mouse models of conditioned reward and psychomotor activation.

**Methods.** Using male C57BL/6J mice, the ability of repeated PEA injections (1 or 10 mg/kg i.p) to modulate the development of a conditioned place preference (CPP) and behavioural sensitization (BS) induced by cocaine (20 mg/kg i.p.) was evaluated. In addition, the expression of cocaine-induced CPP and BS after acute PEA administration was also studied.

**Results.** PEA (1 and 10 mg/kg i.p) significantly reduced the development of cocaine-induced BS, but did not modify the acquisition of cocaine-induced CPP. Furthermore, both doses of PEA were able to reduce the expression of BS and CPP.

**Conclusions.** Altogether, these findings show that exogenous administration of PEA attenuated psychomotor activation and impaired the expression of CPP induced by cocaine. Our results may be relevant in order to understand the role of NAEs in the development and treatment of cocaine addiction.

**Keywords.** Cocaine, palmitoylethanolamide, behavioural sensitization, CPP.

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