Acute administration of palmitoylethanolamide: behavioural studies

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N-palmitoylethanolamide (PEA), the amide of palmitic acid and ethanolamine, belongs to the family of lipidic mediators that includes endogenous ligands of peroxisome proliferator-activated receptor-alpha (PPAR-α). PEA is broadly demonstrated to possess effects on metabolism, feeding, inflammation and pain (Pistis and Melis, 2010). The discovery that PEA is able to prevent nicotine addiction in rats has highlighted the role of these ligands in the modulation of the rewarding properties of nicotine and indicates that PPAR-α might provide a valuable new target for antismoking medications (Mascia et al., 2010). Furthermore, Mazzola and coworkers (2009) have recently proposed the involvement of PPAR-α in learning and memory thus providing new behavioral evidence of a central role of these nuclear receptors. However, the mechanism of PEA action in the brain is largely unknown. Our previous investigations have shown that PEA induces a dose-dependent antidepressant-like effect with a behavioral profile similar to that of the tricyclic antidepressant amitriptyline (unpublished data). This effect was reversed by the PPARα antagonist MK886 showing that it is specifically mediated via PPAR-α activation. Scope of this study was to characterize the pharmacological effects of an acute intraperitoneal (ip) administration of PEA (1-2mg/kg) on anxiety, social interaction and spontaneous motor activity. Anxiety-like behavior has been evaluated by means of the elevated plus maze (EPM) test, that is based on the conflict between the animal's instinct to explore its environment and its innate fear for open spaces: classical anxiolytic drugs elevate the time spent in the open compartments and the number of entries (Pellow and File, 1986). In the EPM test, we found that PEA (1-2 mg/kg ip) did not modify the percentage of either the open arm entries and the time spent in the open arms as compared to vehicle-treated controls. The active social behavior was tested by means of the social interaction (SI) test that could provide another measure of anxiety (File and Seth, 2003) with time spent in social interactions being usually elevated by anxiolytic drugs. Animal acutely treated with 1 mg/kg (ip) of PEA significantly decreased the total social interaction time but did not modify the total numbers of contacts with respect to vehicle-treated controls thus revealing an anxiogenic-like response. In the spontaneous motor activity test, evaluated using the Digiscan Animal Activity Analyser (Omnitech Electronics, USA), we found that horizontal, vertical and center locomotor activities significantly decreased over time in both vehicle and PEA-treated rats (1-2 mg/kg ip) with no difference between treatment groups. Our results add further sustenance to the biological and pharmacological effects demonstrated for PPAR-α agonists, suggesting an anxiogenic-like effect after acute administration. Since several antidepressant drugs show an anxiogenic profile after acute treatment but anxiolytic effects after chronic treatment, it will be important to investigate the pharmacological and behavioral profile of PEA following a chronic regime of treatment.

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