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ROLE OF DOPAMINE D4 RECEPTOR IN THE DEVELOPMENT OF MORPHINE-INDUCED ANALGESIC TOLERANCE

POSTER SESSION 01 - SECTION: PAIN AND INFLAMMATION

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Morphine is one of the most effective drugs used for pain management. However, prolonged exposition to morphine produces effects such as tolerance to analgesia and addiction. Downregulation of the mu opioid receptor (MOR) and its uncoupling to G-proteins in the dorsal horn are likely to contribute to the development of morphine tolerance. Previous studies demonstrated that dopamine D_4 receptor (D_4R) activation prevents morphine addiction by modulating dopamine signaling from nigral dopamine cells. This effect seems to be the result of an antagonistic receptor-receptor interaction involving a D_4R-MOR heteroreceptor which could exist in the dorsal striatum. As D_4R is expressed in dorsal horn neurons, we hypothesize that D_4R could interfere in the development of morphine-induced tolerance to its analgesic effects. Here, using a chronic paradigms of combined treatment of morphine with the D_4R agonist PD168.077, we investigated the nociceptive response to three noxious stimuli: thermal (tail-flick test), mechanical (von Frey test) and chemical (formalin test). Moreover, using immunohistochemical techniques, we have evaluated alterations in the primary circuitry of pain (peptidergic and non-peptidergic C fibers and spinal projections neurons NK1-R) and the balance between glutamate and GABA within dorsal horn. Results from the evaluation of analgesic activity of chronic combined treatment of morphine with PD168,077 showed that D_4R prevents the development of morphine-induced analgesic tolerance. This results give support for the existence of antagonistic functional D_4R-MOR interaction in the dorsal horn that could help to the development of a new pharmacology strategy for treatment of pain. Support: CTS161 and UMA20-FEDERJA-122 (Junta de Andalucía, Spain)