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groups of rats still exhibited a strong hyperalgesia during phase I formalin following administration of each NSAID, an effect not observed in non-tolerant rats. Pretreatment with naloxone completely prevented the analgesic effects of these three NSAIDs in both behavioral assays. In the other study we investigated the development of tolerance to the analgesic effects of NSAIDs diclofenac, ketorolac and xefocam microinjected into the rostral part of anterior cingulate cortex (ACC) in rats. Animals receiving NSAIDs into the ACC were tested for antinociception by tail-flick (TF) and hot plate (HP) tests. Treatment with each NSAID significantly enhanced the TF and HP latencies on the first day, followed by a progressive decrease in the analgesic effect over a 4-day period, i.e., developed tolerance. Pretreatment with an opioid antagonist naloxone completely prevented the analgesic effects of the three NSAIDs in both behavioral assays. These findings support the concept that the development of tolerance to the antinociceptive effects of NSAIDs is mediated via an endogenous opioid system possibly involving descending pain modulatory systems. The present findings support the concept that the development of tolerance to the antinociceptive effects of NSAIDs in acute and inflammatory pain models is mediated via an endogenous opioid system possibly involving descending pain modulatory systems.

Keywords: antinociception, hyperalgesia, mechanical and thermal paw withdrawal, tail-flick, hot plate

RATS' NOCICEPTION UNDER CHRONIC SOCIAL STRESS AND N-STEAROYLETHANOLAMINE ADMINISTRATION

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It is generally accepted that stress-induced analgesia is one of consequences of stress. Endocannabinoids are known to be involved in nociceptive andinflammatory alterations that occur during and after influence of stress. Thus, N-stearoylethanolamine as a substance that influences on bioactive compound of the endocannabinoid system could shift nociception. The aim of the study was to evaluate the effects of N-stearoylethanolamine on flick-tail response of rats under chronic social stress. It has been demonstrated that chronic social stress (two weeks daily resident-intruder agonistic social interactions) led to a significant increase in pain threshold which remained at least two weeks after agonistic social interactions. N-stearoylethanolamine reduced latency of flick-tail response in the near-term period of its appliance. Moreover, two-week daily administration of N-stearoylethanolamine during but not after development of chronic social stress prevented the development of the stress-induced analgesia in rats. The study was done under support of the State Fund For Fundamental Research (grants F64/20-2015 and F64/28-2016).

Keywords: chronic social stress, stress-induced analgesia, endocannabinoids, N-stearoylethanolamine