

## (Anti)Depressant Effects of Non-Steroidal Antiinflammatory Drugs in Mice

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**Abstract :** Purpose: The study aimed to assess the depressant or antidepressant effects of several Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in mice: the selective cyclooxygenase-2 (COX-2) inhibitor meloxicam, and the non-selective COX-1 and COX-2 inhibitors lornoxicam, sodium metamizole, and ketorolac. The current literature data regarding such effects of these agents are scarce. Materials and methods: The study was carried out on NMRI mice weighing 20-35 g, kept in a standard laboratory environment. The study was approved by the Ethics Committee of the University of Medicine and Pharmacy „Carol Davila”, Bucharest. The study agents were injected intraperitoneally, 10 mL/kg body weight (bw) 1 hour before the assessment of the locomotor activity by cage testing (n=10 mice/ group) and 2 hours before the forced swimming tests (n=15). The study agents were dissolved in normal saline (meloxicam, sodium metamizole), ethanol 11.8% v/v in normal saline (ketorolac), or water (lornoxicam), respectively. Negative and positive control agents were also given (amitryptilline in the forced swimming test). The cage floor used in the locomotor activity assessment was divided into 20 equal 10 cm squares. The forced swimming test involved partial immersion of the mice in cylinders (15/9cm height/diameter) filled with water (10 cm depth at 28C), where they were left for 6 minutes. The cage endpoint used in the locomotor activity assessment was the number of treaded squares. Four endpoints were used in the forced swimming test (immobility latency for the entire 6 minutes, and immobility, swimming, and climbing scores for the final 4 minutes of the swimming session), recorded by an observer that was "blinded" to the experimental design. The statistical analysis used the Levene test for variance homogeneity, ANOVA and post-hoc analysis as appropriate, Tukey or Tamhane tests. Results: No statistically significant increase or decrease in the number of treaded squares was seen in the locomotor activity assessment of any mice group. In the forced swimming test, amitryptilline showed an antidepressant effect in each experiment, at the 10 mg/kg bw dosage. Sodium metamizole was depressant at 100 mg/kg bw (increased the immobility score, p=0.049, Tamhane test), but not in lower dosages as well (25 and 50 mg/kg bw). Ketorolac showed an antidepressant effect at the intermediate dosage of 5 mg/kg bw, but not so in the dosages of 2.5 and 10 mg/kg bw, respectively (increased the swimming score, p=0.012, Tamhane test). Meloxicam and lornoxicam did not alter the forced swimming endpoints at any dosage level. Discussion: 1) Certain NSAIDs caused changes in the forced swimming patterns without interfering with locomotion. 2) Sodium metamizole showed a depressant effect, whereas ketorolac proved antidepressant. Conclusion: NSAID-induced mood changes are not class effects of these agents and apparently are independent of the type of inhibited cyclooxygenase (COX-1 or COX-2). Disclosure: This paper was co-financed from the European Social Fund, through the Sectorial Operational Programme Human Resources Development 2007-2013, project number POSDRU /159 /1.5 /S /138907 "Excellence in scientific interdisciplinary research, doctoral and postdoctoral, in the economic, social and medical fields -EXCELIS", coordinator The Bucharest University of Economic Studies.

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