(Anti) depressant effects of non-steroidal anti-inflammatory drugs in mice

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INTRODUCTION

- Forced swimming test (FST) or Porsolt test is very useful in the detection of antidepressant properties of different classes of substances.
- An important part of non-steroidal anti-inflammatory drugs (NSAIDs) is scarcely studied regarding their (anti) depressant properties.
- Data from literature:
  - In FST and also in tail suspension test (TST) performed in rats, aspirin, piroxicam, celecoxib, and ibuprofen showed serum antidepressant effects [1-3].
  - In TST and FST performed in mice with “sickness behaviour” (after bacillus Calmette-Guérin or endotoxin inoculation), ibuprofen, indomethacin, nimesulide, naproxen, and rofecoxib showed antidepressant effects [4-6].
  - On other hand, ketoprofen showed depressant effect per se effects, while ibuprofen, naproxen, aspirin and acetaminophen antagonized the antidepressant effects of selective serotonin reuptake inhibitors [7, 8].

OBJECTIVES

- To assess the depressant or antidepressant effects of several NSAIDs in mice: the selective cyclooxygenase-2 (COX-2) inhibitor meloxicam, and the non-selective COX-1 and COX-2 inhibitors ibuprofen, sodium metamizol, and ketorolac. The potential sedative or psychomotor stimulating effect was also assessed.

MATERIALS & METHODS

- NMRI mice (n=10-15).
- The tests performed: exploration of locomotor activity in a special cage (in order to exclude a sedative or psychomotor stimulating effect) and forced swimming test (in order to assess the influences on the mood).
- Exploration of locomotor activity
  - Substances and doses:
    - Meloxicam 5 mg/kg and 10 mg/kg, ibuprofen 2.5 mg/kg and 5 mg/kg
    - Sodium metamizol 25 mg/kg, 50 mg/kg, and 100 mg/kg
    - Ketorolac 2.5 mg/kg, 5 mg/kg, and 10 mg/kg.
  - All administered 1 hour before the tests.
- Acrylic plastic cages illuminated with light from the ceiling of the room were used. The cage floor was divided into 20 equal 10 cm squares. The cage arena was cleaned following each trial.
  - Endpoint used: number of squares traversed by mice in 5 minutes.
- Forced swimming test
  - Substances and doses:
    - Meloxicam 5 mg/kg and 10 mg/kg, ibuprofen 2.5 mg/kg and 5 mg/kg
    - Meloxicam 1.25 mg/kg, 2.5 mg/kg, and 5 mg/kg (a second experiment)
    - Sodium metamizol 25 mg/kg, 50 mg/kg, and 100 mg/kg.
    - Ketorolac 2.5 mg/kg, 5 mg/kg, and 10 mg/kg.
  - Administered 2 hours before the tests.
  - All experiments: amitriptyline 10 mg/kg, administered 30 minutes before the tests.
- The test equipment consisted of Berzelius glasses 18 cm high, 10 cm diameter, water height 12 cm, water temperature 28°C, and video recording systems. The experiments were carried out in daylight conditions, between 08:30 and 16:30 hours.
- Endpoints used: immobility latency across 6 minutes, and 5-second intervals' scoring of the last 4 minutes of immobility, swimming, and climbing respectively (thus resulting in 48 scoring intervals for each animal). The method was described by Costa AP et al., 2013 [9].
- Statistics: normality tests of the results' distribution, homogeneity of variance tests, ANOVA, and parametric post hoc tests – the Tukey test (based on homogenous dispersion), and the Tamhane test (not involving homogenous dispersion). P<0.05 indicated a statistically significant difference.