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## Effects of ketoprofen, morphine, and kappa opioids on pain-related depression of nesting in mice.

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**Abstract:** Pain-related functional impairment and behavioral depression are diagnostic indicators of pain and targets for its treatment. Nesting is an innate behavior in mice that may be sensitive to pain manipulations and responsive to analgesics. The goal of this study was to develop and validate a procedure for evaluation of pain-related depression of nesting in mice. Male ICR mice were individually housed and tested in their home cages. On test days, a 5- × 5-cm Nestlet was subdivided into 6 pieces, the pieces were evenly distributed on the cage floor, and Nestlet consolidation was quantified during 100-minute sessions. Baseline nesting was stable within and between subjects, and nesting was depressed by 2 commonly used inflammatory pain stimuli (intraperitoneal injection of dilute acid; intraplantar injection of complete Freund adjuvant). Pain-related depression of nesting was alleviated by drugs from 2 classes of clinically effective analgesics (the nonsteroidal anti-inflammatory drug ketoprofen and the  $\mu$ -opioid receptor agonist morphine) but not by a drug from a class that has failed to yield effective analgesics (the centrally acting kappa opioid agonist U69,593). Neither ketoprofen nor morphine alleviated depression of nesting by U69,593, which suggests that ketoprofen and morphine effects were selective for pain-related depression of nesting. In contrast to ketoprofen and morphine, the kappa opioid receptor antagonist JD1c blocked depression of nesting by U69,593 but not by acid or complete Freund adjuvant. These results support utility of this procedure to assess expression and treatment of pain-related depression in mice.