

Monosodium Iodoacetate Model of Osteoarthritis Pain

The rat monosodium iodoacetate (MIA) model is a model of osteoarthritis in which intraarticular injection of MIA (3 - 4.5 mg) into the left hindlimb knee joint results in cartilage degeneration, localized inflammation, and pain behaviors. Pain behaviors commonly measured in this model include hind paw mechanical allodynia and weight bearing deficits, and this model is commonly used to evaluate the efficacy of compounds for pain associated with osteoarthritis of the knee joint.

Behavioral Pain Phenotype: Hind Paw Weight Bearing Deficits

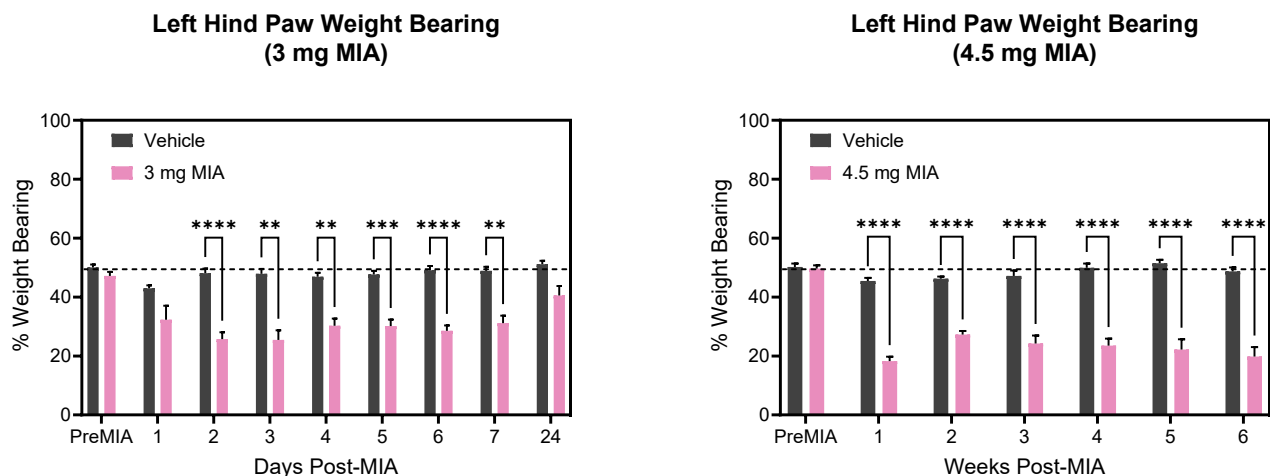


Figure 1: Development of transient (*left*) and persistent (*right*) weight bearing deficits on the left hind paw following intraarticular injection of 3 or 4.5 mg MIA into the left hindlimb knee joint, respectively. Decreased weight bearing is maximal from Days 2 – 7 following injection of 3 mg MIA, and this effect is no longer observed by Day 24. Decreased weight bearing is maximal in Week 1 following injection of 4.5 mg MIA, and weight bearing deficits are observed through Week 6.

% Weight Bearing = Left hind paw weight bearing / (Left + Right hind paw weight bearing) X 100.

**** $p < 0.0001$, ** $p < 0.01$ Bonferroni's test; $n = 7-10$ /group

Pharmacology: Morphine and Ketoprofen Reduce Hind Paw Weight Bearing Deficits

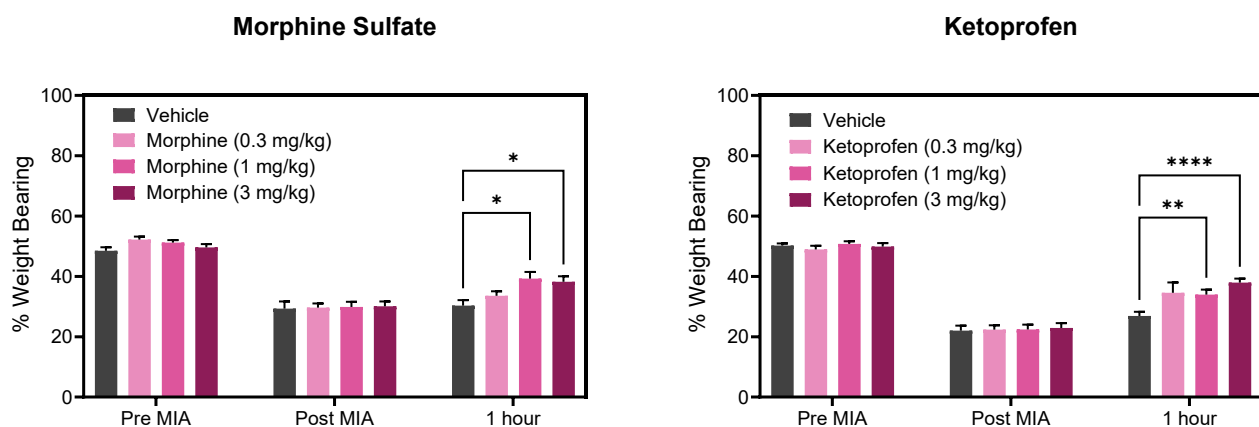


Figure 2: Reduction of weight bearing deficits following administration of morphine (*left*) and ketoprofen (*right*). Effects of single administration of morphine on MIA (3 mg/kg)-induced weight bearing deficits were determined on Day 6 at 1-hour post-dosing, and effects of repeated administration of ketoprofen (Days 3-6, b.i.d.) on weight bearing deficits were determined on Day 6 at 1-hour post-dosing. **** $p < 0.0001$, ** $p < 0.01$, * $p < 0.05$ Dunnett's test; $n = 9-12$ /group

Behavioral Pain Phenotype: Hind Paw Mechanical Allodynia

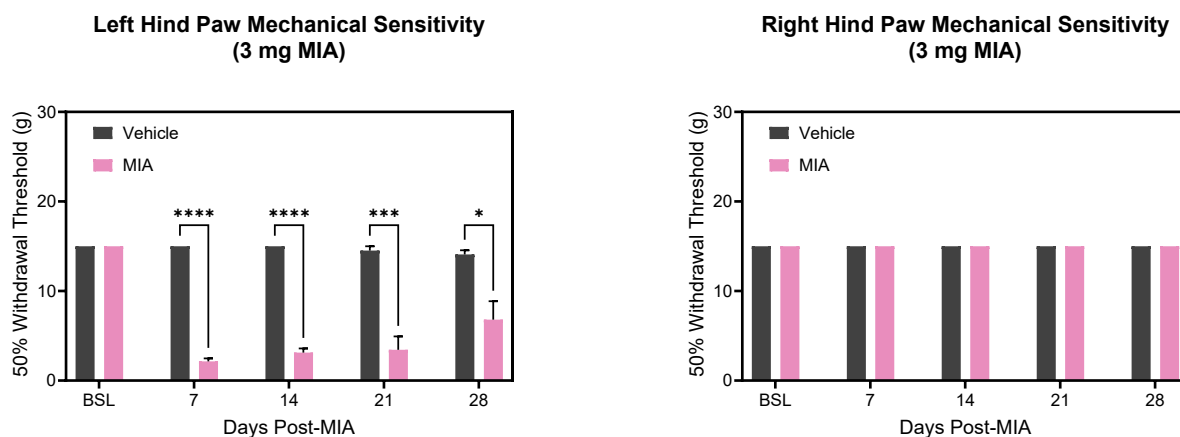


Figure 3: Development of hind paw mechanical allodynia on the left hind paw following intraarticular injection of 3 mg MIA into the left hindlimb knee joint. Mechanical allodynia on the left hind paw is maximal during the first week (Day 7) with some recovery observed by Day 28. Right hind paw mechanical sensitivity is unaffected by MIA injection into the left hindlimb knee joint. Mechanical allodynia is represented as decreased 50% withdrawal thresholds to von Frey filament stimulation.

**** $p < 0.0001$, *** $p < 0.001$, * $p < 0.05$ Bonferroni's test; $n = 10/\text{group}$

Pharmacology: Morphine but not Ketoprofen Reduces Hind Paw Mechanical Allodynia

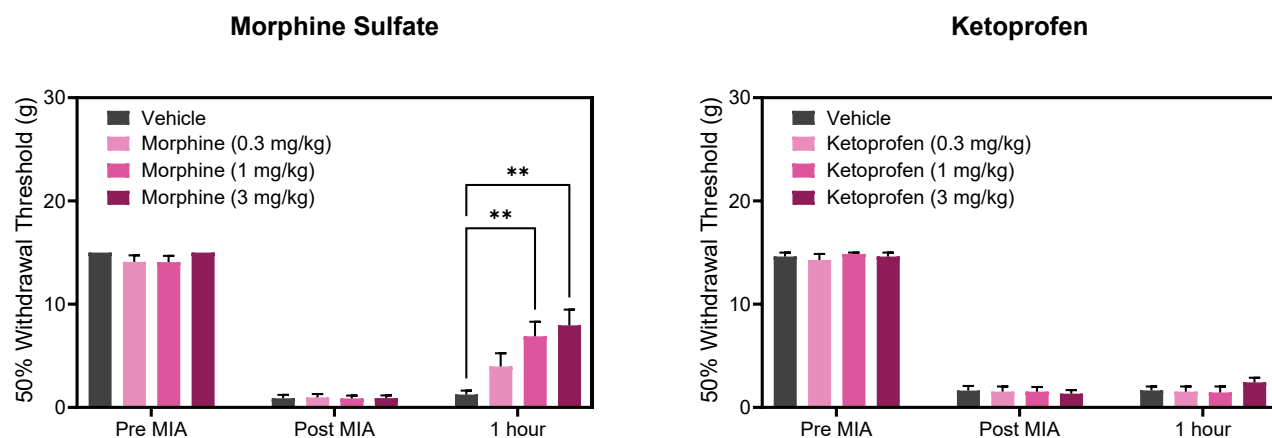


Figure 4: Reduction of hind paw mechanical allodynia following administration of morphine (left) but not ketoprofen (right). Effects of single administration of morphine on mechanical allodynia were determined on Day 8 at 1-hour post-dosing, and effects of repeated administration of ketoprofen (Days 5-8, b.i.d.) on mechanical allodynia were determined on Day 8 at 1-hour post-dosing. Mechanical allodynia is represented as decreased 50% withdrawal thresholds to von Frey filament stimulation.

** $p < 0.01$, Dunnett's test; $n = 8-10/\text{group}$