Characterization of the Rat Monoiodoacetate Model of Osteoarthritis: Evoked and Non-evoked Pain Response Assessments

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Intraarticular injection of monoiodoacetate (MIA) into the rat knee joint results in joint degeneration indicative of osteoarthritis (OA). In collaboration with the NIH HEAL Initiative Preclinical Screening Platform for Pain (PSPP) we evaluated various evoked and non-evoked pain endpoints in the rat MIA model.

Adult male and female Sprague Dawley rats were injected with MIA (0.3 – 3 mg/kg), and tactile sensitivity, pinch sensitivity and weight bearing were measured for 4-6 weeks. Following pain phenotyping, pharmacological validation of the model was established using various analgesics. Intraarticular injection of MIA (1 and 3 mg) into the hindlimb knee joint produced unilateral hind paw tactile hypersensitivity which was maximal at Week 2 post MIA injection, and female rats also showed knee hypersensitivity to pinch stimuli. Modest and pronounced weight bearing deficits were observed when measuring static and dynamic weight bearing, respectively.

A single dose of morphine (6 mg/kg, s.c.) reduced hind paw tactile hypersensitivity and weight bearing deficits, whereas a single dose of ketoprofen (6 mg/kg, p.o.) or duloxetine (60 mg/kg, p.o.) was ineffective. Repeated dosing with ketoprofen or duloxetine (4 days, b.i.d.) significantly reduced tactile hypersensitivity and weight bearing deficits. The results from this study demonstrate that single and repeated treatment paradigms may be used to identify and differentiate novel therapeutics for osteoarthritis pain.