Title: THE NIH HEAL INITIATIVE PRECLINICAL SCREENING PLATFORM FOR PAIN (PSPP) VALIDATION OF THE MONOIODOACETATE (MIA) MODEL OF OSTEOARTHRITIS PAIN IN THE RAT

Authors:
S. Woller [1], M. Urban [2], T. Hanania [2], S. Iyengar [1]
[1]NINDS, Rockville, United States, [2]PsychoGenics Inc., Paramus, United States

Main Category: T (translational)

Main Topic: Pharmacological therapies

Background and aims: The National Institutes of Health Helping to End Addiction Long-term[SM] Initiative, or NIH HEAL Initiative[SM], Preclinical Screening Platform for Pain (PSPP) aims to accelerate the discovery and development of non-opioid, non-addictive pain therapeutics. PSPP is collaborating with PsychoGenics, Inc. to validate preclinical models and endpoints to enable screening and profiling of assets. Here, we describe the optimization and validation of the rat monoiodoacetate (MIA) model of osteoarthritis pain.

Methods: The left hindlimb knee joint of adult male and female Sprague Dawley rats (N=10, each sex) was injected intraarticularly with MIA (0.3 – 3 mg). Tactile sensitivity, weight bearing, gait, and knee pressure were systematically evaluated longitudinally. Pharmacological validation of the model was established using morphine (3 mg/kg), duloxetine (60 mg/kg), and ketoprofen (6 mg/kg) after acute and repeated dosing.

Results: Intraarticular injection of MIA produced unilateral hind paw tactile hypersensitivity, changes in gait, and deficits in dynamic weight bearing in both sexes. Female, but not male, rats showed hypersensitivity to pressure and pinch stimuli. Subcutaneous injection of morphine reduced hind paw tactile hypersensitivity and weight bearing deficits in both sexes, whereas acute oral administration of ketoprofen and duloxetine were less effective. In contrast, repeated treatment with ketoprofen or duloxetine (4 days, b.i.d.) significantly reduced tactile hypersensitivity and weight bearing deficits.

Conclusions: The results suggest that both tactile sensitivity and dynamic weight bearing in the acute and repeated treatment paradigms of the rat MIA model may be used to identify and differentiate novel therapeutics for treatment of osteoarthritis within the HEAL Initiative's PSPP program.