PsychoGenics
Transforming CNS Discovery

Paclitaxel Model of Chemotherapy-Induced Peripheral Neuropathy

Paclitaxel is a commonly used chemotherapeutic agent in the taxane class which can produce neurotoxicity and sensory neuropathy in patients, often reported as numbness, tingling, or burning pain. A rat model of paclitaxel-induced sensory neuropathy has been established in which paclitaxel (4 mg/kg, IP) is administered to SD rats on alternate days (Day 1, 3, 5, 7) resulting in long-term (>6 weeks) cold and mechanical allodynia in the hind paws. The paclitaxel model is commonly used to evaluate the efficacy of compounds for pain associated with chemotherapeutic agents in the taxane class.

Behavioral Pain Phenotype: Bilateral Hind Paw Cold and Mechanical Allodynia

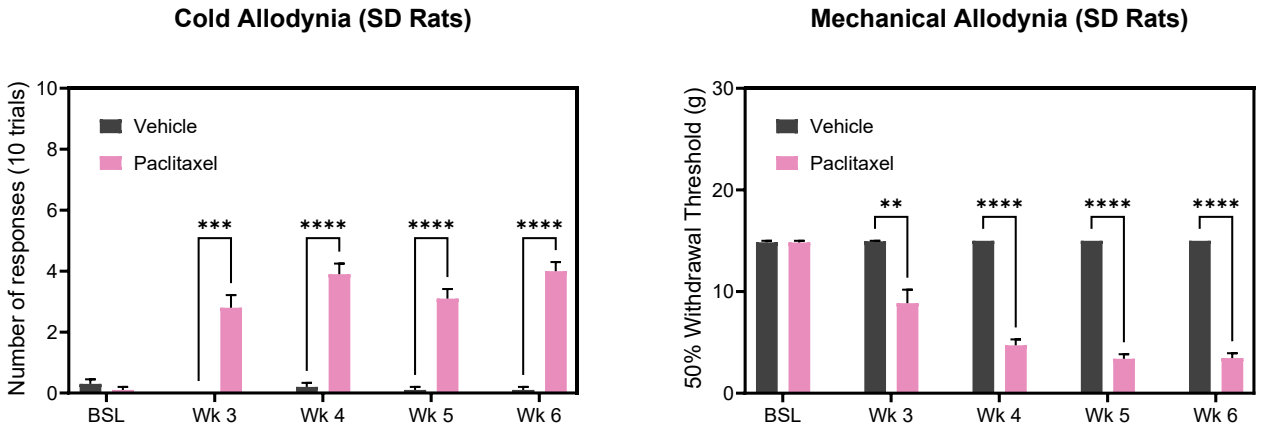

Figure 1: *Development of bilateral hind paw cold* ***(left)*** *and mechanical* ***(right)*** *allodynia during Weeks 3 – 6 following paclitaxel (4 mg/kg, IP) or vehicle (EtOH/Cremophor/saline; 1:1:4, IP) administration on Days 1, 3, 5, 7 (Week 1). Cold allodynia is represented as increased number of withdrawal responses to acetone application (5 applications left/right hind paw; total 10 applications), and mechanical allodynia is represented as decreased 50% withdrawal thresholds to von Frey filament stimulation (average of left and right hind paw). **** p<0.0001, *** p<0.001, ** p< 0.01*

Pharmacology: Morphine Reduces Hind Paw Cold and Mechanical Allodynia

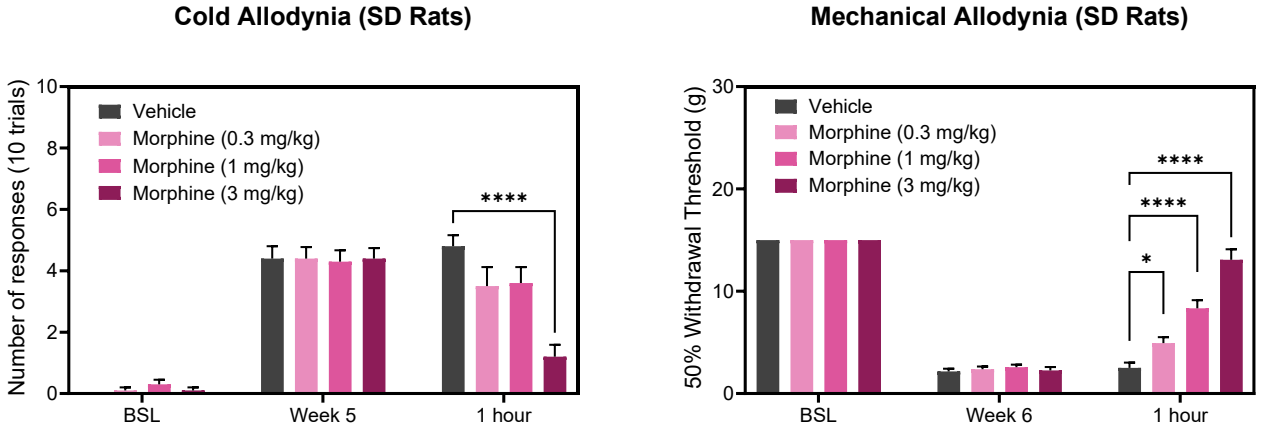

Figure 2: *Bilateral hind paw cold* ***(left)*** *and mechanical* ***(right)*** *allodynia in SD rats prior to paclitaxel treatment (BSL), prior to dosing (Week 5, Week 6) and 1 hour following dosing with morphine sulfate (SC), or vehicle (SC).*
***** p<0.0001, * p<0.05, Dunnett's test*

PsychoGenics
Transforming CNS Discovery

Oxaliplatin Model of Chemotherapy-Induced Peripheral Neuropathy

Oxaliplatin is a commonly used chemotherapeutic agent in the platinum-complex class which can produce sensory neuropathy, including neuropathic pain. A rat model of oxaliplatin-induced neuropathy has been established in which oxaliplatin (3 mg/kg, IV) is administered over a period of 4 weeks (2 days per week, total 8 doses) resulting in hind paw cold and mechanical allodynia which persists for > 8 weeks. The oxaliplatin model is commonly used to evaluate the efficacy of compounds for the treatment of pain associated with platinum-based chemotherapeutic agents.

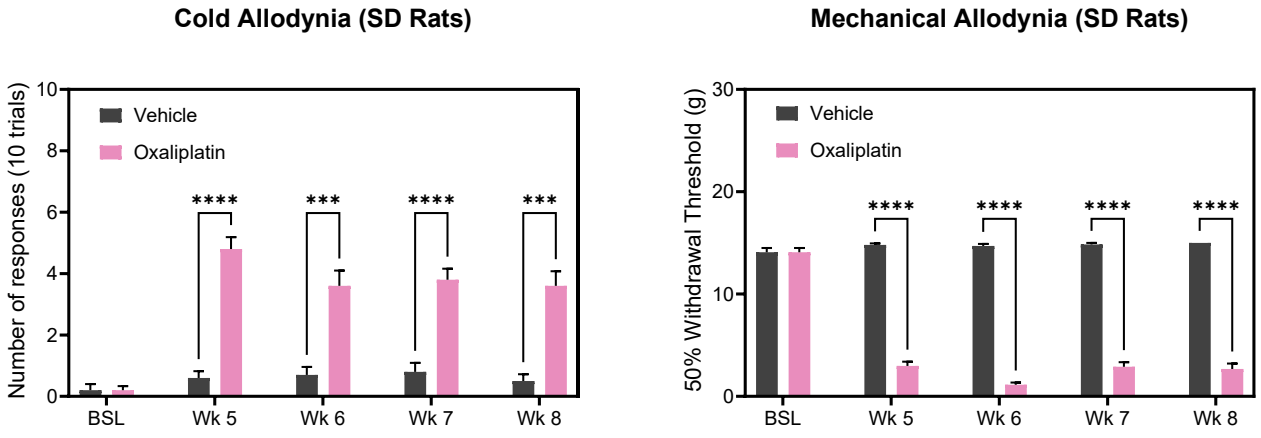

Figure 3: *Development of bilateral hind paw cold* ***(left)*** *and mechanical* ***(right)*** *allodynia during Weeks 5 – 8 following oxaliplatin (3 mg/kg, IV) or vehicle (saline, IV) administration during Weeks 1-4 (2 days per week). Cold allodynia is represented as increased number of withdrawal responses to acetone application (5 applications left/right hind paw; total 10 applications), and mechanical allodynia is represented as decreased 50% withdrawal thresholds to von Frey filament stimulation (average of left and right hind paw). **** p<0.0001, *** p<0.001, ** p< 0.01*

Pharmacology: Morphine Reduces Hind Paw Cold and Mechanical Allodynia

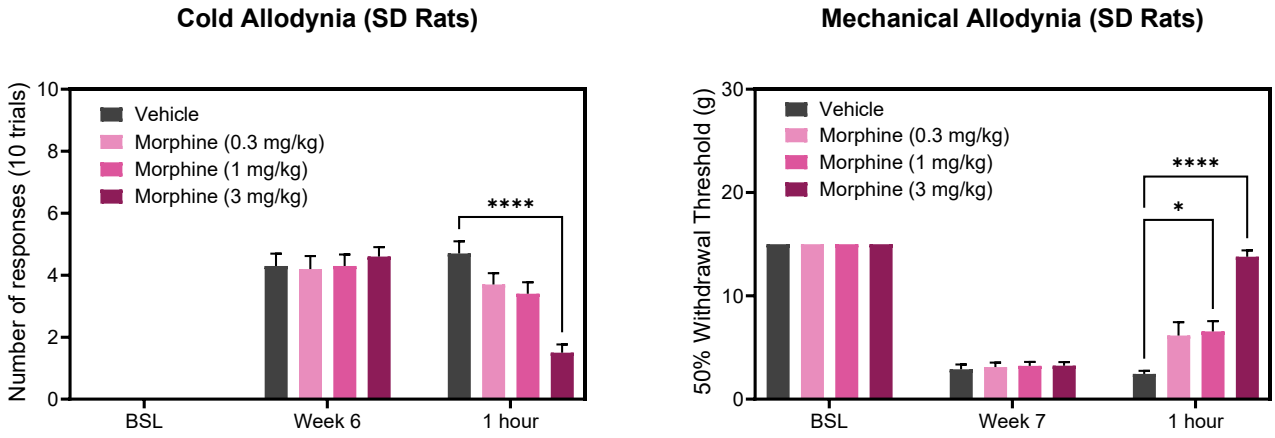

Figure 4: *Bilateral hind paw cold* ***(left)*** *and mechanical* ***(right)*** *allodynia in SD rats prior to oxaliplatin treatment (BSL), prior to dosing (Week 6, Week 7) and 1- hour following dosing with morphine sulfate (SC), or vehicle (SC).*
***** p<0.0001, * p<0.05, Dunnett's test*