

Surgical Models of Neuropathic Pain

Spinal Nerve Ligation Model

Spinal nerve ligation (SNL) is a model of peripheral neuropathic pain resulting from chronic nerve compression. This L5/L6 SNL model produces a robust, long-term pain phenotype in rats, resulting in mechanical and cold allodynia in the hind paw ipsilateral to the SNL surgery. This phenotype mimics symptoms seen in human neuropathic pain conditions such as nerve compression syndrome and post-herpetic neuralgia. The SNL model is commonly used to investigate the mechanisms of chronic neuropathic pain and evaluate the efficacy of compounds for neuropathic pain.

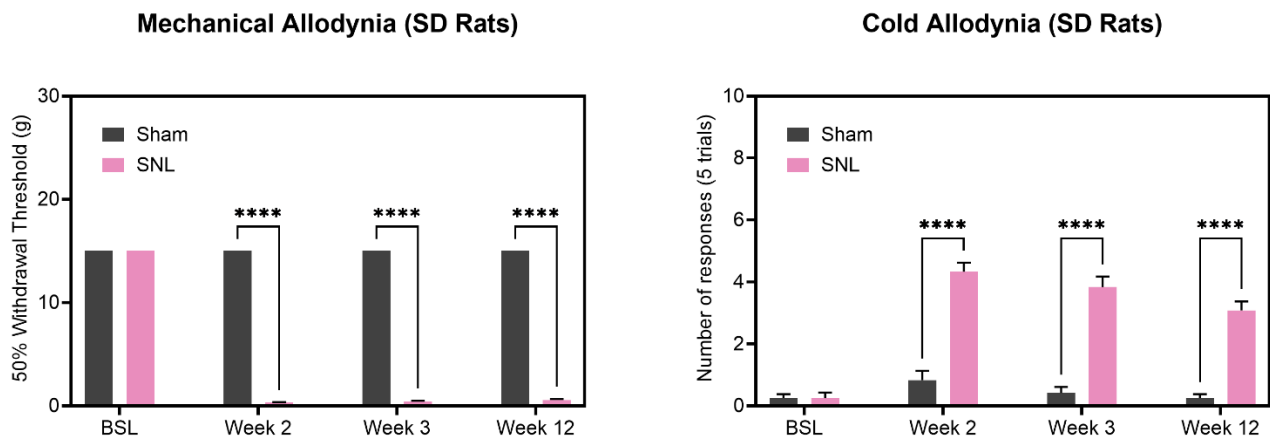


Figure 1: Development of ipsilateral hind paw mechanical (*left*) and cold (*right*) allodynia during Weeks 2 – 12 following the spinal nerve ligation or sham procedure. Mechanical allodynia is represented as decreased 50% withdrawal thresholds to von Frey filament stimulation and cold allodynia is represented as increased number of withdrawal responses to acetone application (5 applications to the ipsilateral hind paw). **** $p < 0.0001$

Pharmacology: Gabapentin Reduces Hind Paw Mechanical and Cold Allodynia

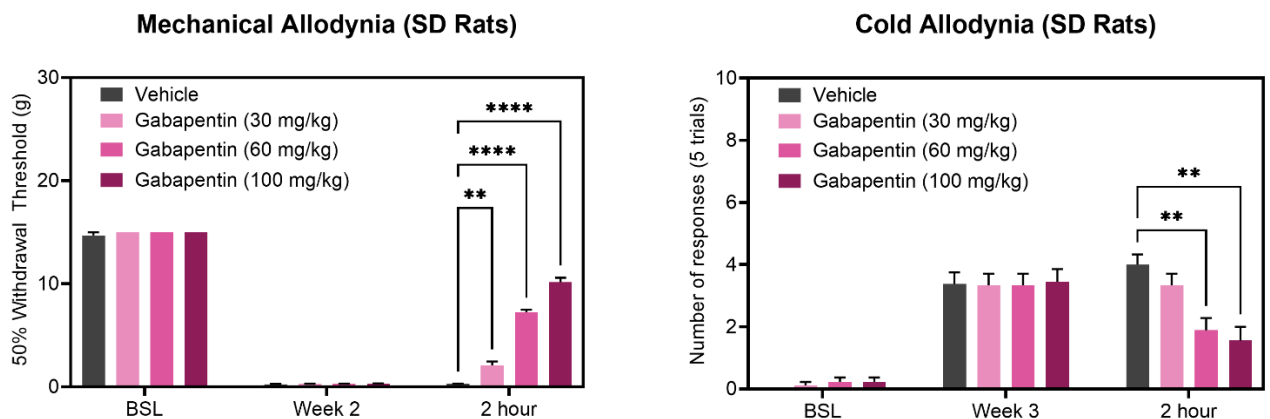


Figure 2: Ipsilateral hind paw mechanical (*left*) and cold (*right*) allodynia in SD rats prior to SNL surgery (BSL), prior to dosing (Week 2, Week 3) and 2 hours following dosing with gabapentin (PO), or vehicle (PO).

**** $p < 0.0001$, ** $p < 0.01$, Dunnett's test

Spared Nerve Injury Model

The spared nerve injury (SNI) model is a model of peripheral neuropathic pain in which the common peroneal and tibial nerves are ligated and axotomized, while the sural nerve remain intact. The resulting neuropathy produces robust hind paw mechanical allodynia which is maximal by Day 7 and can persist for > 6 months. This model is unique in that differences in sensitivity thresholds may be examined in the hind paw innervated by the intact sural nerve and injured nerves. The SNI model may be used to investigate the mechanisms of chronic neuropathic pain associated with axotomy and to evaluate the efficacy of compounds for neuropathic pain.

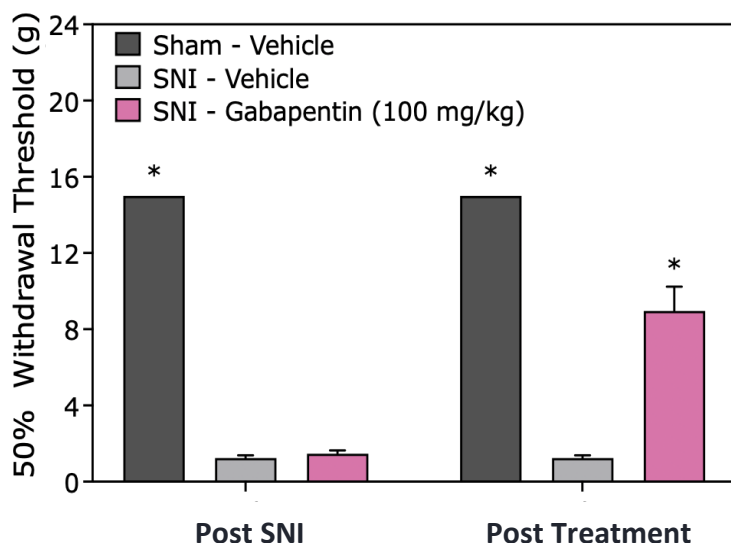


Figure 3: In the spared nerve injury (SNI) model hind paw mechanical allodynia is observed in SD rats 2 weeks post-surgery compared to rats that received a sham surgical procedure. Administration of gabapentin (100 mg/kg, PO) reduced hind paw mechanical allodynia at 1-hour post-dosing in the SNI model.

* $p < 0.05$

Chronic Constriction Injury

The chronic constriction injury (CCI) model is a model of peripheral neuropathic pain in which 3-4 chromic gut ligatures are loosely tied around the common sciatic nerve at the level of the mid-thigh. This model results in a localized neuroinflammation around the injured area of the sciatic nerve involving immune cell infiltration, intraneural edema, and focal ischemia. The behavioral pain phenotype associated with this model included of mechanical and cold allodynia. The CCI model may be used to investigate the mechanisms of chronic neuropathic pain associated with neuroinflammation and to evaluate the efficacy of compounds for neuropathic pain.

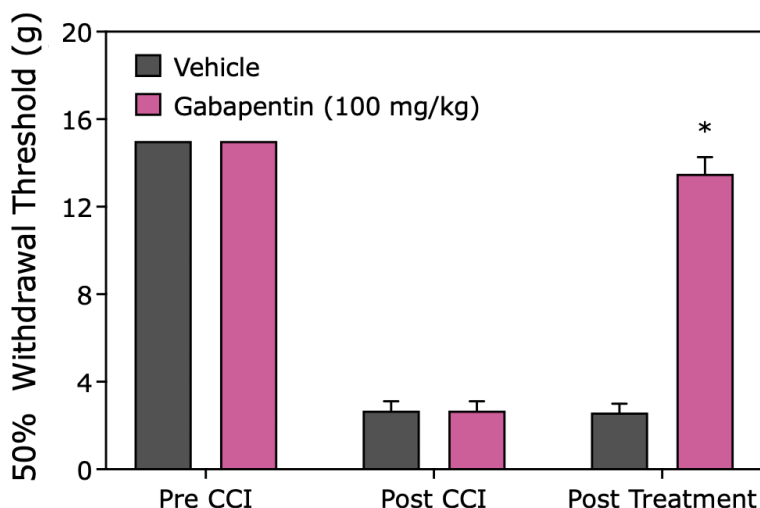


Figure 4: In the chronic constriction injury (CCI) model hind paw mechanical allodynia is observed in SD rats 2 weeks post-surgery. Administration of gabapentin (100 mg/kg, PO) reduced hind paw mechanical allodynia at 1-hour post-dosing in the CCI model.

* $p < 0.05$