



Prophylactic versus Delayed Surgical Intervention for the Prevention of Symptomatic Neuromas



Purpose

Neuroma formation following peripheral nerve injury often results in persistent, debilitating neuropathic pain. Surgical approaches such as regenerative peripheral nerve interfaces and vascularized denervated muscle targets (VDMTs) attempt to prevent and treat symptomatic neuromas. The prevailing notion amongst clinicians is that any intervention (VDMT, RPNI, etc.) at the time of nerve injury as prophylaxis against neuromas is more successful in reducing pain than intervention performed to treat a symptomatic neuroma. This study evaluated how prophylactic versus delayed intervention after the onset of chronic pain changes behavioral manifestations of pain in a rodent VDMT model.

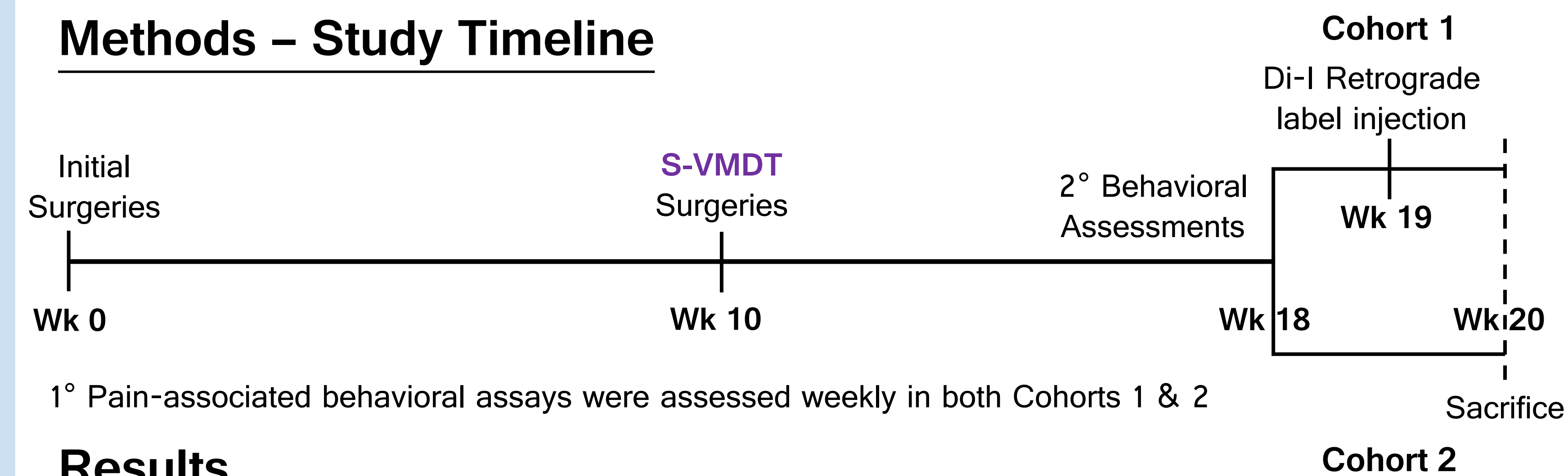
Hypothesis

In the setting of nerve transection, intervention performed immediately (**Primary VDMT; P-VDMT**) will allow regenerating axons to reinnervate denervated muscle targets and therefore prevent neuroma formation. Delayed intervention after neuroma formation (**Secondary VDMT; S-VDMT**) will be less effective in reducing pain behaviors due to pre-established central sensitization secondary to neuroma formation

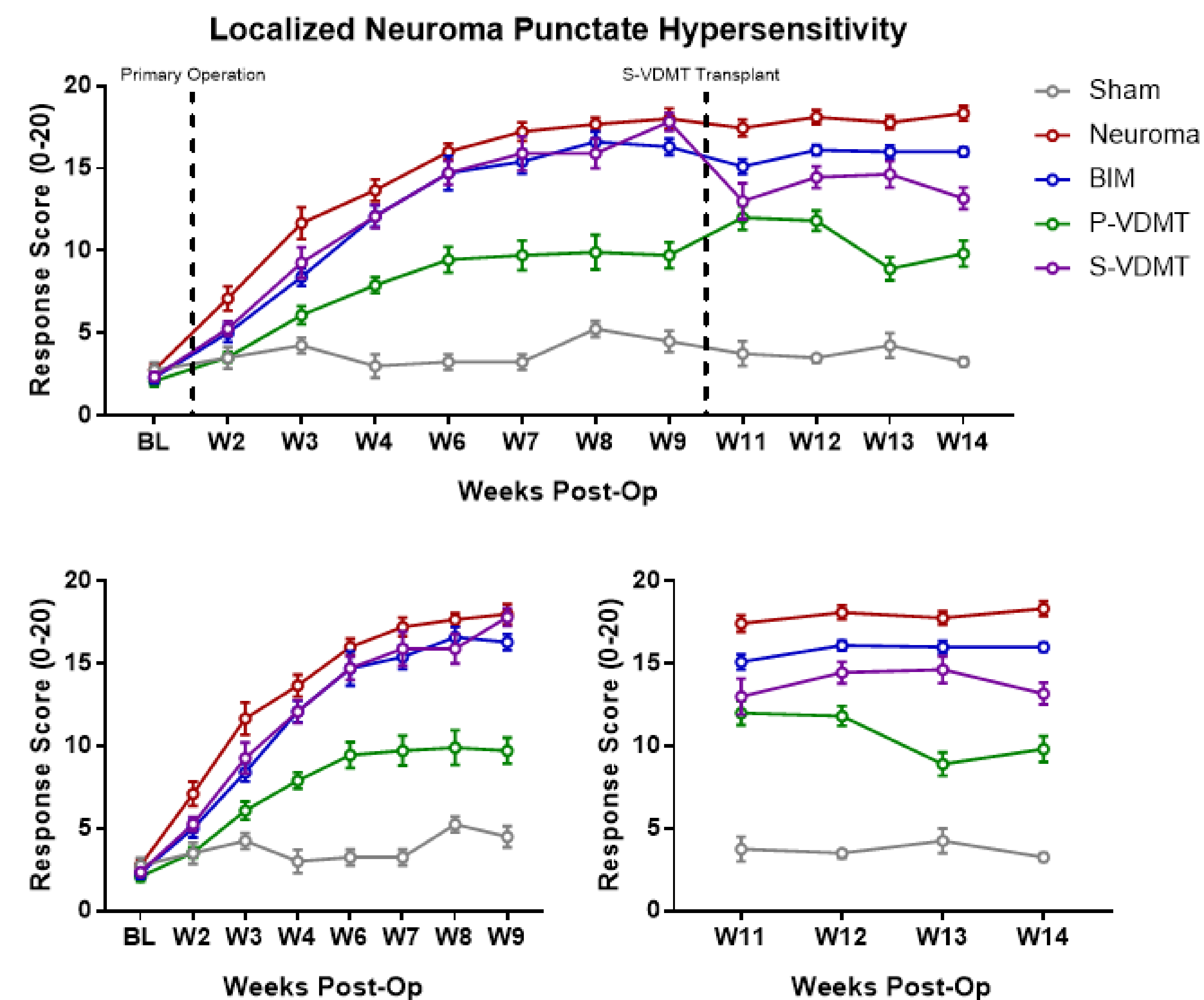
Methods – Study Groups

- **Sham**
- **Neuroma**: The peroneal nerve was transected and unrepaired
- **Bury-in-Muscle (BIM)**: The transected personal was sutured into innervated lateral gastrocnemius muscle
- **P-VDMT**: The transected peroneal nerve was sutured into the denervated lateral gastrocnemius muscle, and the muscle was wrapped around the nerve, a vascular leash was maintained
- **S-VDMT**: The peroneal nerve was transected, 10 weeks later the neuroma was excised and a VDMT was created

Methods – Study Timeline



Results



Conclusions

Our findings demonstrate prophylactic intervention provides the greatest prevention against symptomatic neuroma formation. Additionally, regardless of timing, denervated muscle targets provide greater benefit than innervated targets. Histologic and transcriptomic analyses are currently ongoing.

Methods – Outcomes

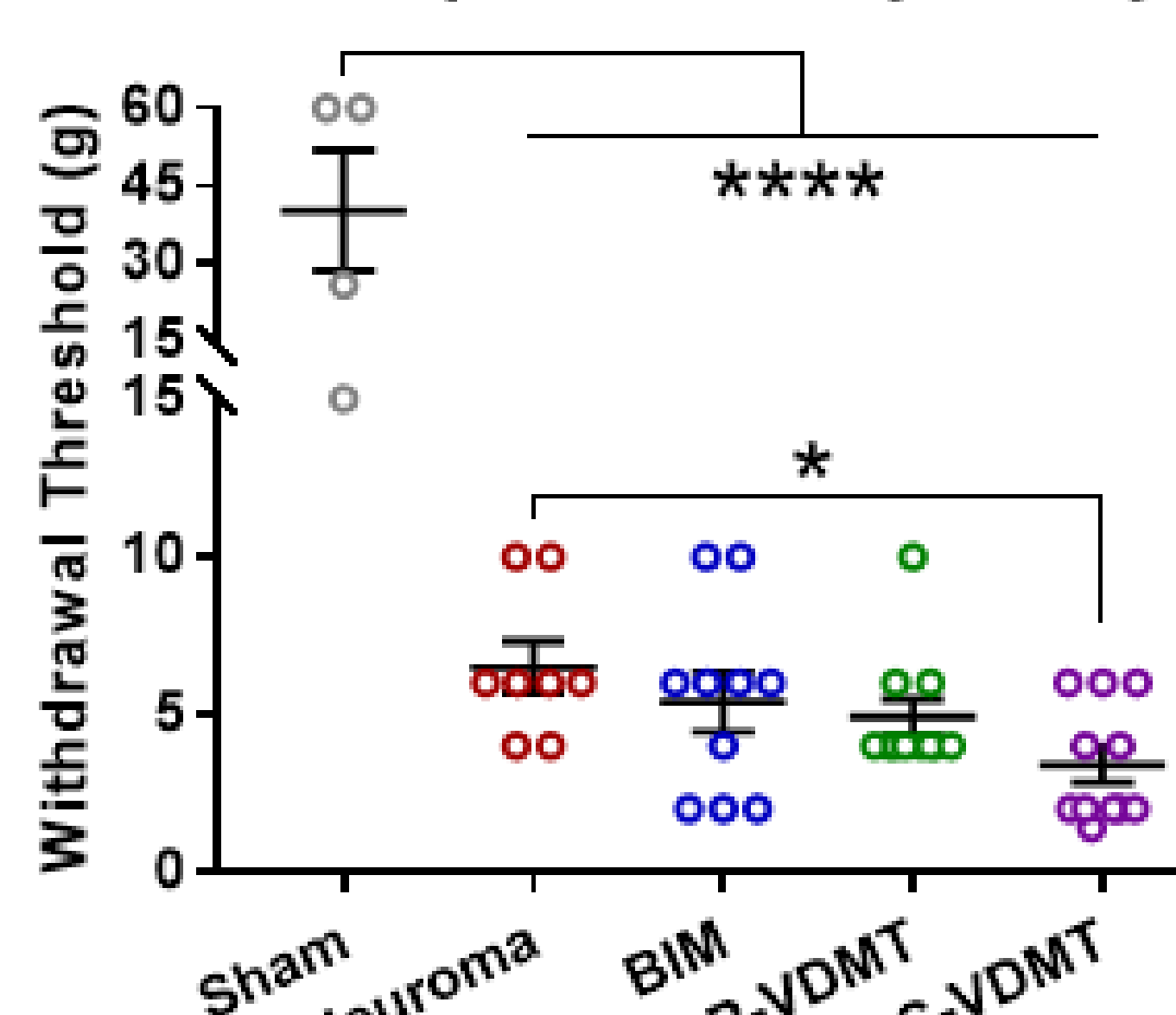
Cohort 1 – Histological Assessment:

- Pain and regeneration associated markers in the dorsal root ganglia
- Axonal growth & neuroma formation
- Density/percent reinnervation of motor endplates

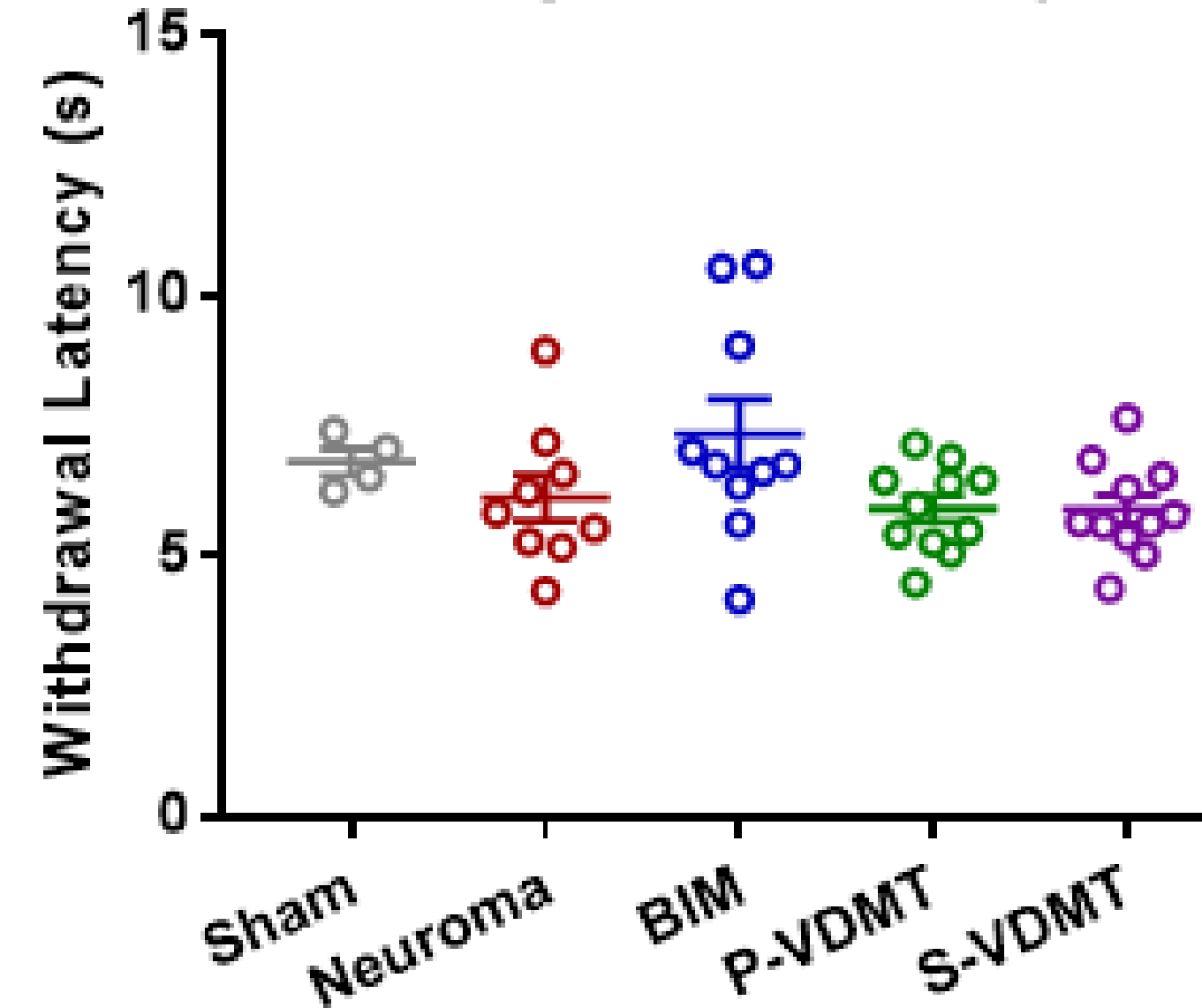
Cohort 2 – RNA Sequencing:

- L3-L5 dorsal root ganglia were collected for next generation RNA sequencing

Hindpaw Von Frey Assay



Hargreave's Assay



A) Upon localized neuroma punctate hypersensitivity assessment, **P-VDMT** animals demonstrated reduced primary mechanical allodynia compared to all other interventions prior to **S-VDMT** intervention ($p < 0.0001$). After **S-VDMT** intervention at Week 10, **S-VDMT** animals demonstrated reduced primary mechanical allodynia compared to **BIM** ($p < 0.01$); however, both **S-VDMT** and **BIM** scored significantly lower than **Neuroma** animals ($p < 0.001$). **P-VDMT** continued to demonstrate reduced allodynia compared to all other interventions through Week 19 ($p < 0.01$).

B) **S-VDMT** animals demonstrated significantly more severe secondary hindpaw mechanical allodynia compared to **Neuroma** ($p < 0.05$) and **Sham** animals ($p < 0.0001$).

C) All groups displayed similar levels of thermal sensitivity.