

INTRODUCTION

Reliable preclinical spinal cord injury (SCI) models are essential for developing new therapies, but setting up an SCI lab is costly and requires specialized expertise. These barriers often deter researchers and investors from entering the field.

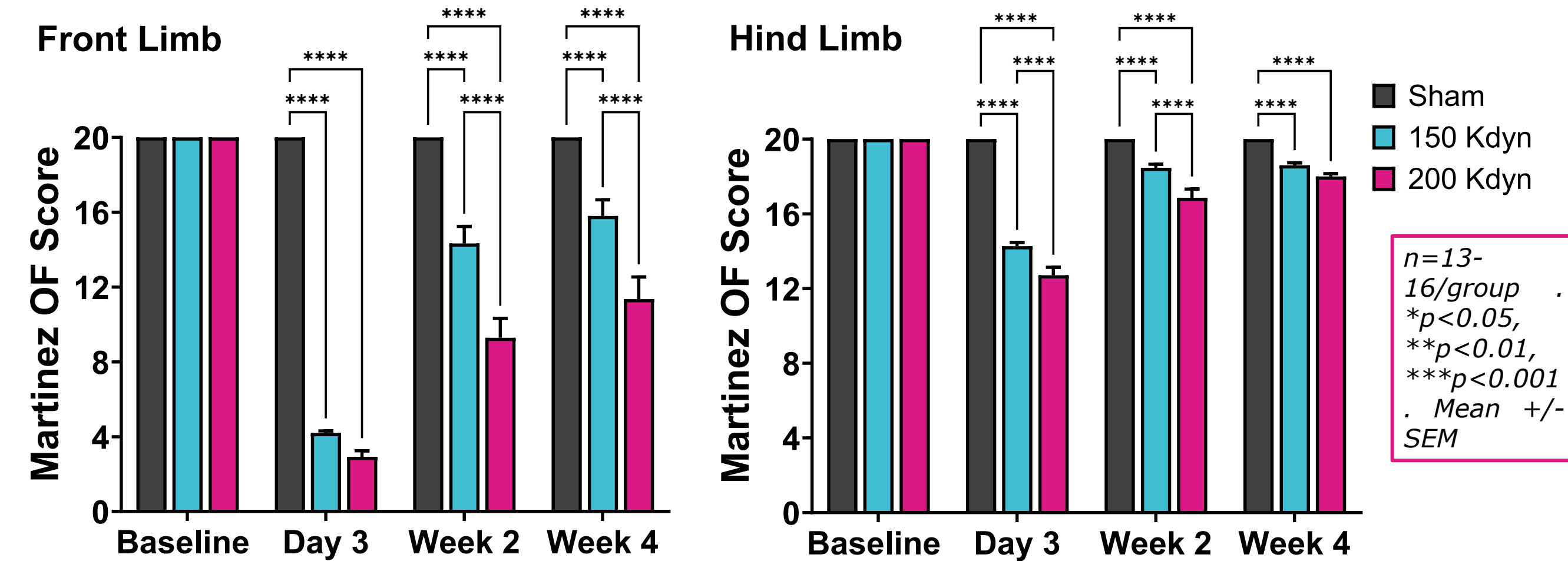
To address this, PsychoGenics, in collaboration with the Christopher & Dana Reeve Foundation and Drexel University, validated standardized models of Cervical contusion SCI. A specialized SCI-focused Contract Research Organization (CRO) can streamline research, reduce costs, and enable consistent evaluation of potential treatments.

METHODS

- Subjects & Surgeries.** Adult, female, Sprague Dawley rats (180-220 grams, Envigo) underwent laminectomy on the right side of the Cervical 5 vertebrae, followed by contusion SCI using the IH impactor with forces of either 150 or 200Kdyn.
- Functional recovery** was assessed at baseline and over five weeks after SCI using standard locomotor tests, including the Irvine, Beattie, and Bresnahan (IBB) rating scale (Irvine, 2014), the Martinez Open Field Score (Martinez, 2009), Horizontal Ladder test (Metz and Whishaw, 2009), Paw Placement preference test, Lever Pull assay and PsychoGenics' proprietary gait analysis system, NeuroCube® (NC). **Sensory function** was evaluated using the Von Frey and acetone tests to measure changes in mechanical and thermal sensitivity, respectively.
- Sample Collection & Immunohistochemistry.** After behavior testing, at 6 weeks after SCI, cerebrospinal fluid and plasma was collected. Three cm sections containing the lesioned spinal cord at its center were cryoprotected, sectioned and stained with fluoromyelin to evaluate lesion size, and spared white matter.
- Statistics.** One-way or Two Way RM ANOVA followed by Tukey's post-hoc test were used, data is presented as Mean +/- SEM.

RESULTS

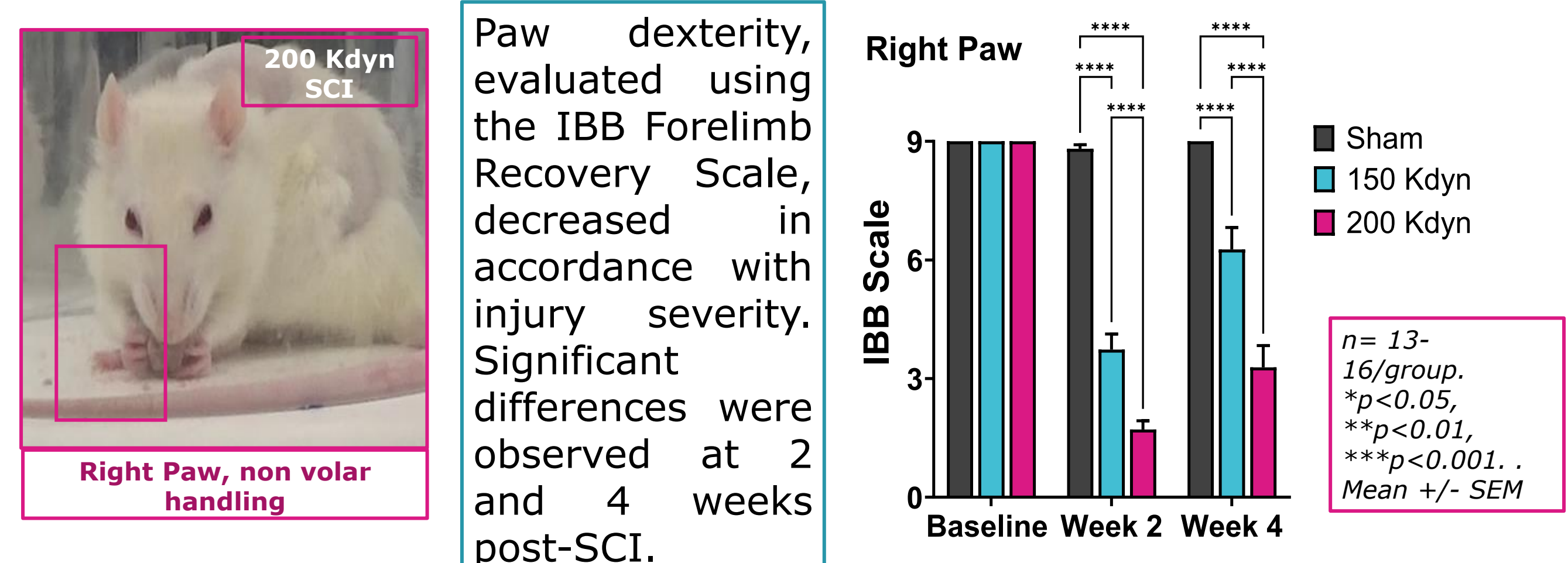
Right Front and Right Hind Limb Locomotion Performance Decreased with Unilateral Cervical SCI



Gross locomotion skills decreased with SCI, primarily on the Right Front Limb. Modest but significant changes are observed in the right Hind Limbs as well.

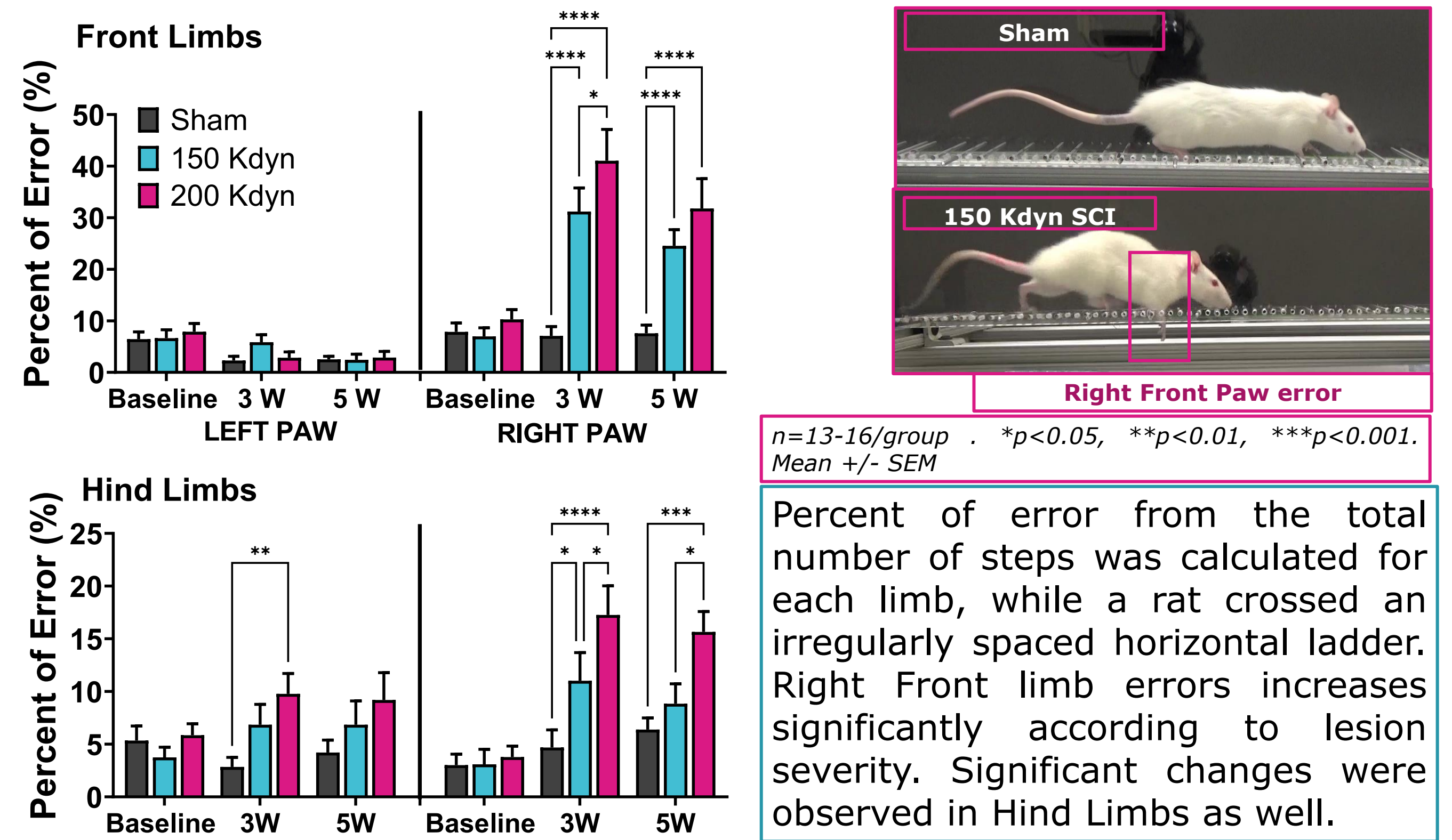


Right Paw dexterity, while handling a pellet, decreased with unilateral Cervical SCI



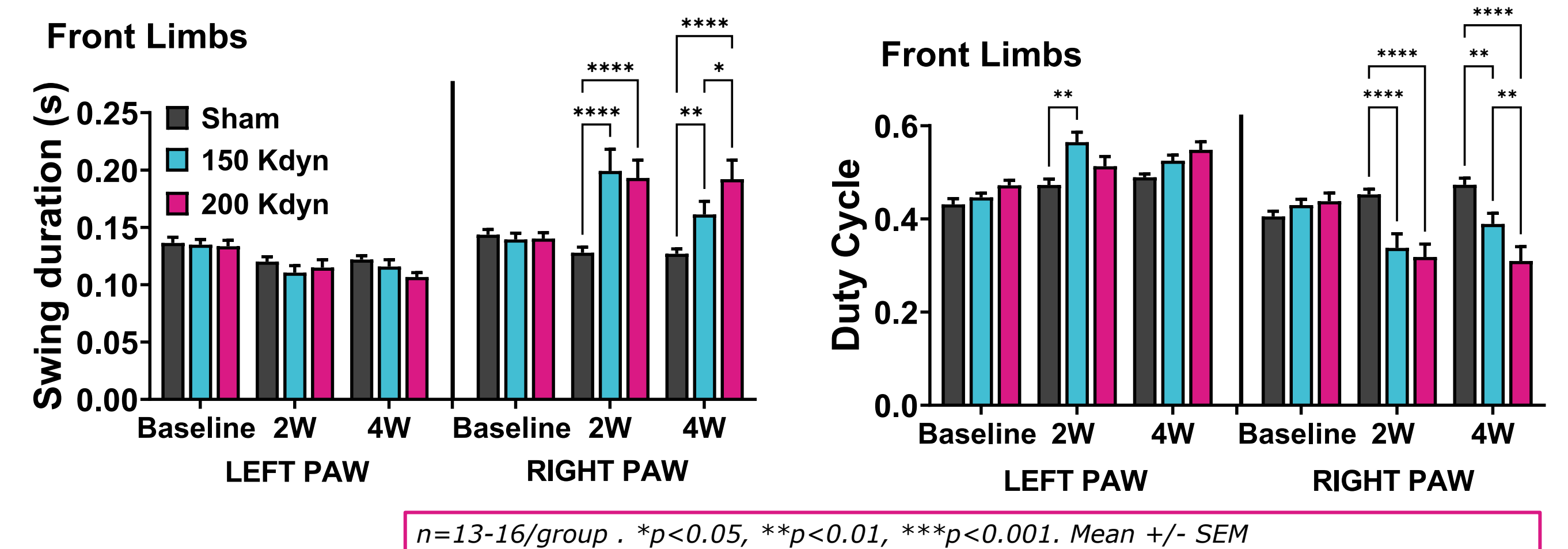
Paw dexterity, evaluated using the IBB Forelimb Recovery Scale, decreased in accordance with injury severity. Significant differences were observed at 2 and 4 weeks post-SCI.

Cervical SCI Severity Impacted Right Front and Hind Limbs Sensorimotor Function



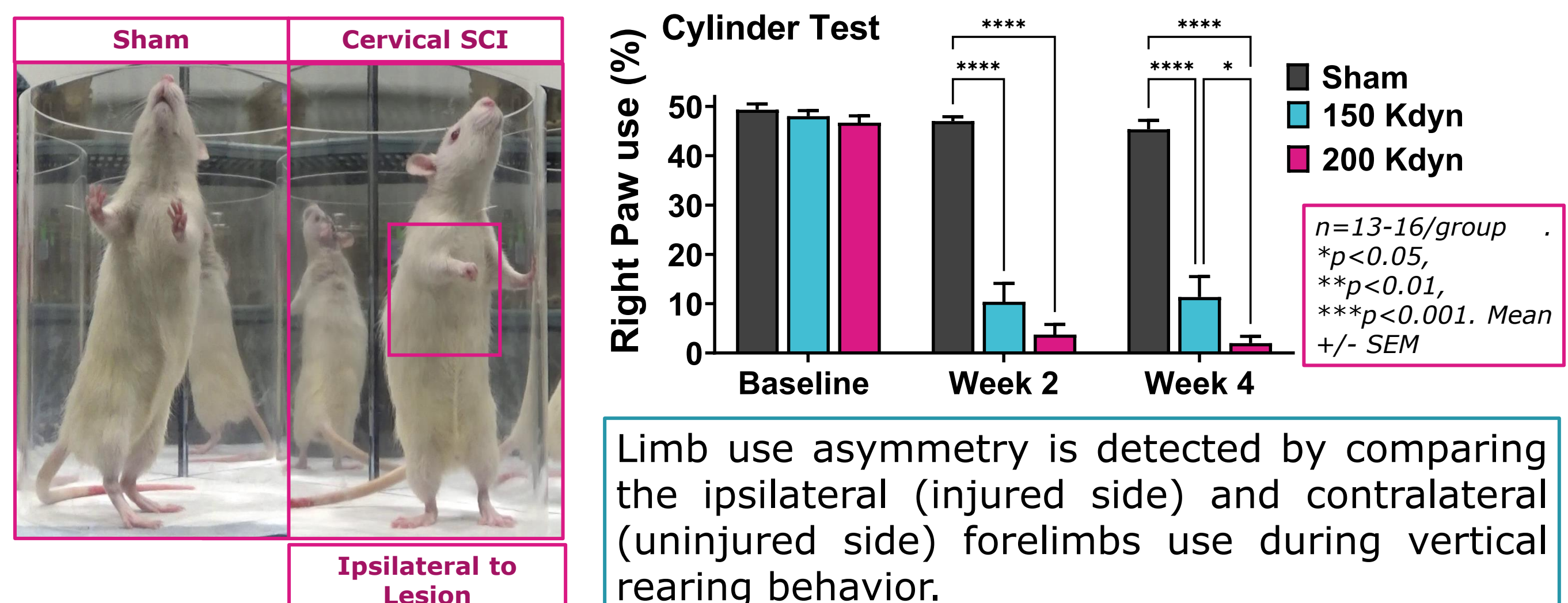
Percent of error from the total number of steps was calculated for each limb, while a rat crossed an irregularly spaced horizontal ladder. Right Front limb errors increases significantly according to lesion severity. Significant changes were observed in Hind Limbs as well.

Unbiased Gait Analysis Using NeuroCube®.



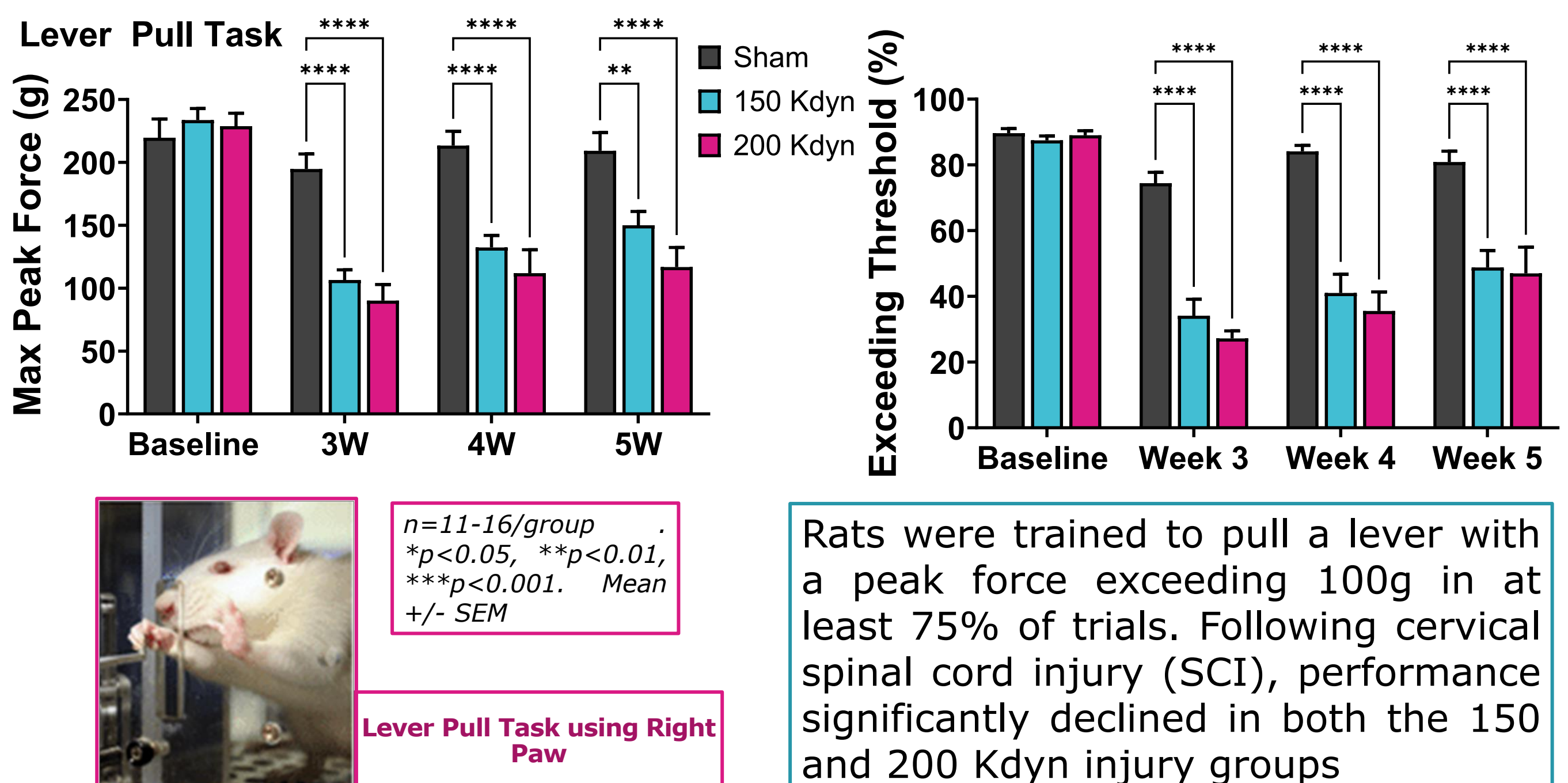
Unilateral cervical SCI increases swing duration in the right forepaw in a manner proportional to injury severity. The duty cycle, which represents the proportion of each step cycle during which the paw bears weight, decreases in the right forepaw with increasing lesion severity.

Cervical SCI Severity Impacted Paw Placement Preference, evaluated by the Cylinder Test



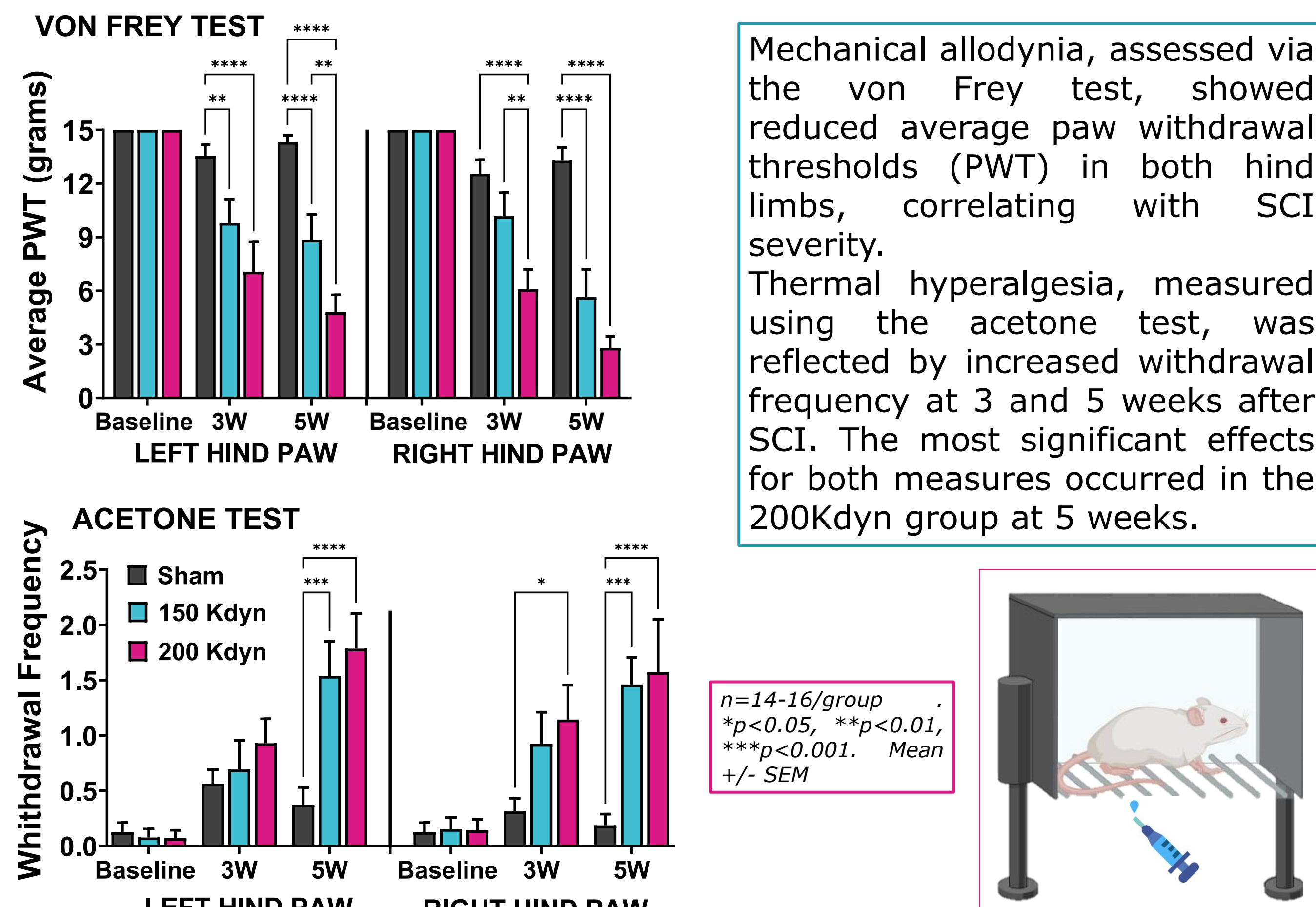
Limb use asymmetry is detected by comparing the ipsilateral (injured side) and contralateral (uninjured side) forelimbs use during vertical rearing behavior.

Forelimb Strength Assessed via Pull Lever Operant Task



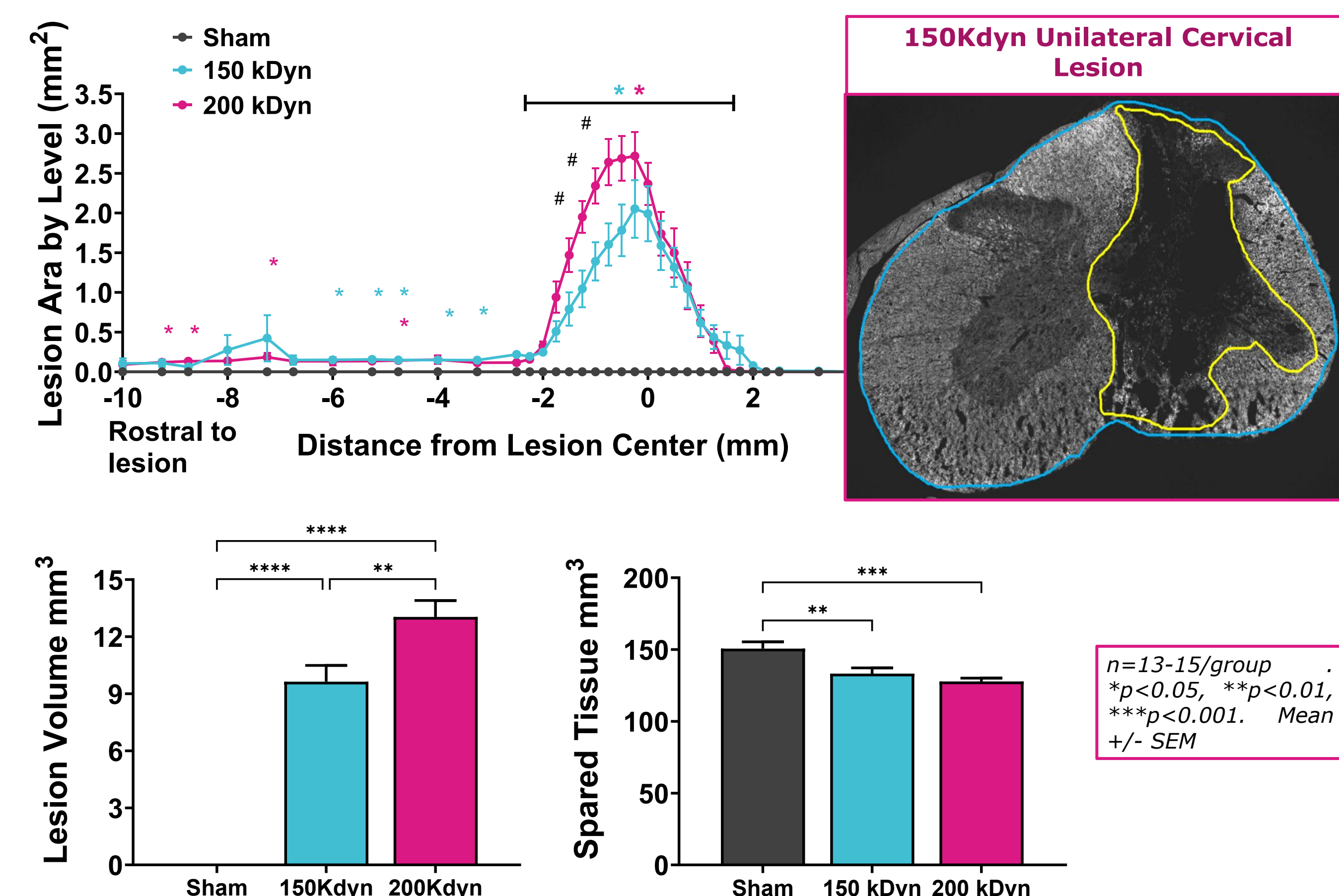
Rats were trained to pull a lever with a peak force exceeding 100g in at least 75% of trials. Following cervical spinal cord injury (SCI), performance significantly declined in both the 150 and 200 Kdyn injury groups

Neuropathic Pain Development in the Hind Paws after Unilateral Cervical SCI



Mechanical allodynia, assessed via the von Frey test, showed reduced average paw withdrawal thresholds (PWT) in both hind limbs, correlating with SCI severity. Thermal hyperalgesia, measured using the acetone test, was reflected by increased withdrawal frequency at 3 and 5 weeks after SCI. The most significant effects for both measures occurred in the 200Kdyn group at 5 weeks.

Histological Evaluation of Lesion and Spared Tissue Size



A 3 cm spinal cord segment containing the lesion epicenter was transversely sectioned and stained with FluoroMyelin. Lesioned area and volume at the epicenter increased with SCI severity, with lesion volume significantly differing between injury groups. Conversely, spared white matter volume decreased with severity, though differences between groups were not statistically significant.

SUMMARY

- The PsychoGenics platform for SCI research supports large-scale studies, with the capacity to test 30-40 animals per week across multiple behavioral assays, capturing multiple aspects of recovery following SCI.
- Unilateral cervical SCI has been validated at two severity levels, each resulting in distinct recovery profiles. The most sensitive behavioral assessments have been identified.
- Gross locomotion, fine locomotion, coordination, gait and paw dexterity are measured using sensitive behavioral tests.
- Changes in mechanical and cold sensitivity demonstrated the association of SCI with allodynia and hyperalgesia.
- Lesion size and spared tissue were quantified through histological analysis.
- This comprehensive SCI platform enhances the ability to evaluate a wide range of drug applications across diverse functional outcomes.