Intervertebral foraminal fibrosis and spinal nerve tethering in a laminectomy rat model

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Introduction: A rat model of the human post-laminectomy condition has been developed and published [1]. In this study, we intend to clarify the following in this model: 1) the effect of laminectomy and disc-injury in the creation of fibrosis within the intervertebral foramen; 2) the ability of hyaluronate to decrease intervertebral foraminal fibrosis; 3) the correlation between fibrosis within the intervertebral foramen and pain behavior (tactile allodynia).

Materials and Methods: Thirty-eight age-matched 400+ grams male Harlan Sprague-Dawley rats were used for the study, and divided into four groups: normal controls (twelve, “Control”), surgical bilateral L5-L6 laminectomies via posterior midline incision (eight, “Lami”), surgical bilateral L5-L6 laminectomies with right-sided L5-6 disc injury using a stereotyped insertion of 27-gauge needle (ten, “Lami-Disc”), and surgical bilateral L5-L6 laminectomies with right-sided L5-6 disc injury with 0.1 cc of topical high molecular weight hyaluronate layered over the dura prior to wound closure (eight, “HA”). The VA Institutional Animal Care Use Committee approved the research protocol.

Pain Behavior Testing Method
Withdrawal thresholds (50% probability) were assessed using calibrated von Frey filaments (Stoelting, Wood Dale, IL) with buckling forces between 4.0-148mN (0.41-15.10g) using a previously published method [2]. As published previously, we used a deviation from normal (15.10g withdrawal threshold) at the eighth week as an indicator of tactile allodynia [3].

Biomechanics Method
Intervertebral foraminal fibrosis of the right L5 spinal nerve was quantified using a biomechanical methodology measuring the load-to-failure as the intact nerve is pulled free from the intervertebral foramen [4]. The nerve was displaced distally at a constant velocity of 1 cm/min along the axis of the spinal nerve and load-to-failure was measured.

Statistical significance (p < 0.05) was evaluated with ANOVA (Statview 5.0, SAS Institute, Cary, NC) and we used appropriate correction for multiple comparisons (Fisher’s LSD). The mean load-to-failure for the right L5 nerve was compared between surgical groups, and also compared between animals with and without tactile allodynia.

Results: All surgical animals survived eight weeks until sacrifice. One HA animal, three Lami animals, and seven Lami-Disc animals showed a withdrawal threshold of less than 15 grams, indicating tactile allodynia.

The load-to-failure of the right L5 spinal nerve was not different between surgical animals with and without tactile allodynia, but surgical animals with (p<0.05) and without (p=0.0005) tactile allodynia had higher load-to-failure compared with the control group.

Discussion: This biomechanical methodology of intervertebral foraminal fibrosis helps quantify the degree of tethering of the spinal nerve to surrounding structures, helping elucidate the pathoanatomy of sciatic pain in the post-laminectomy condition. Surgical laminectomy creates quantifiable fibrosis within the intervertebral foramen. The Lami-Disc group did show a trend towards a significantly higher load-to-failure of the L5 spinal nerve when compared to the Lami group, indicating that disc injury may play an important role in the creation of intervertebral foraminal fibrosis. Disc herniation and injury, such as in human disc surgery, has been shown to liberate pro-inflammatory cytokines that begin the fibrotic cascade and play an important role in neurogenic pain [5]. Hyaluronate is a modulator of inflammation used in ophthalmologic surgery, and has been studied for reducing epidural fibrosis [6]. The HA group did show a trend towards decreasing fibrosis compared to the Lami-Disc group, but statistical significance was not reached. By our power analysis, fifty-two animals per group would be required to show significance. Interestingly, we found that pain behavior did not correlate with an increase in quantifiable fibrosis within the intervertebral foramen. Previous studies have demonstrated a higher number of animals with pain in the Lami-Disc group [1]. A more dynamic test of pain, involving movement of the animal and subsequent stretch on the tethered spinal nerve prior to testing, may be required to consistently detect pain in this model. This current study underscores that surgical laminectomy creates quantifiable fibrosis in the intervertebral foramen, and highlights the possible role of modulators of inflammation for prevention of fibrosis.


Acknowledgements: VA Merit Grant #0003