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The Role of Mechanical Deformation in Lumbar Radiculopathy

An *In Vivo* Model

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Study Design. *In vivo* strain techniques were used in an animal radiculopathy model.

Objective. To quantify the severity of compressive nerve root injury and characterize its effect on resultant mechanical allodynia in a lumbar radiculopathy model.

Summary of Background Data. Clinical and experimental work indicate many factors contributing to radicular pain mechanisms, including mechanical injury. Although it has been suggested that the degree of mechanical injury to the nerve root affects the nature of the pain response, no study has quantified local *in vivo* injury biomechanics, nor have such measures been linked with the resulting magnitude of mechanical allodynia or other clinical symptoms.

Methods. Male Holtzman rats were divided into a sham group with only nerve root exposure or a ligation group in which the nerve root was tightly ligated with a single silk suture. Using image analysis, nerve root radial strains were calculated at the time of injury and after surgery. The animals were grouped according to ligation strain for analysis. Mechanical allodynia was continuously assessed throughout the study.

Results. Compressive strains in the nerve root ranged from 7.8% to 61% (mean, 30.8% ± 14.5%). Animals undergoing larger ligation strains exhibited heightened mechanical allodynia after injury. This was significant using a 12-g von Frey filament ($P = 0.05$). After surgery, the nerve roots displayed tissue swelling, which was relatively uniform in the low-strain group and less so in the high-strain group.

Conclusions. For the first time, *in vivo* biomechanical analysis of tissue deformations was used to investigate the role of mechanics in radicular pain. Overall mechanical allodynia was greater for more severe nerve root injuries (greater strains) in an animal model, suggesting that mechanical deformation plays an important role in the pain mechanism. Continued work is underway to understand the complex interplay between mechanics and the physiology of radicular pain. [Key words: biomechanics, lumbar radiculopathy, nerve root, pain, strain] **Spine 2002;27:27–33**

Low back pain affects as many as two thirds of the adult population in Western society.[4] It is a tremendously costly problem, with estimated annual costs ranging from $38 to $50 billion (U.S.).[5,6] However, despite its high incidence and large cost to society, the current understanding of this and other pain states is incomplete.

Low back pain associated with lumbar radiculopathy results from a complicated combination of neurologic, biochemical, vascular, structural, genetic, and mechanical factors.[16,21,26,27] Although it is commonly agreed that all of these factors play a role in the etiology of lumbar radiculopathy, the relative contribution of the individual components remains uncharacterized. Specifically, the relation of mechanical injury and local tissue mechanics to pain responses is unknown.

Clinically, mechanical compression of the lumbar spinal nerve roots and dorsal root ganglions, either by disc prolapse or spinal stenosis, may lead to lumbar radiculopathy. As such, experimental studies imposing nerve root compression *via* balloon inflation at the cauda equina have been performed to relate mechanical compression to overall *in vivo* neurologic function. Olmarker et al[17,19] and Pedowitz et al[20] reported that increases in the magnitude and duration of tissue compression were associated with increased edema formation and decreased electrical impulse propagation. Multilevel cauda equina compression in a dog model also has produced transient decreases in measured conduction velocity.[15] In the rat, after occlusion of the spinal and foraminal canals, electrophysiologic recordings indicated altered conduction responses, and behavior testing showed decreased ambulation.[12,28]

Although these studies suggest a relation between compression and physiologic functionality, they have not provided quantitative measurements of loading to individual neural structures of the central nervous system, such as the nerve root. In addition, the local mechanics of individual tissues have not been characterized during the gross injuries imposed on them. Although balloon inflation pressure has been reported to characterize the load delivered to the cauda equina, the mechanical environment of individual nerve roots and other anatomic structures has not been described. Without quantification of the local mechanics that may directly initiate an injury response, the role of mechanical injury in lumbar radiculopathy will remain uncertain.

Limited experimental studies implicate mechanical deformation as a mechanism of physiologic damage measured by alterations in the electrophysiology and structure of neural tissue after compression and unloading.[2,8,23,29] Lundborg et al[14] and Rydevik et al[22] showed that endoneurial pressure increases in the regions of compressed rat sciatic nerve and dorsal root ganglion.

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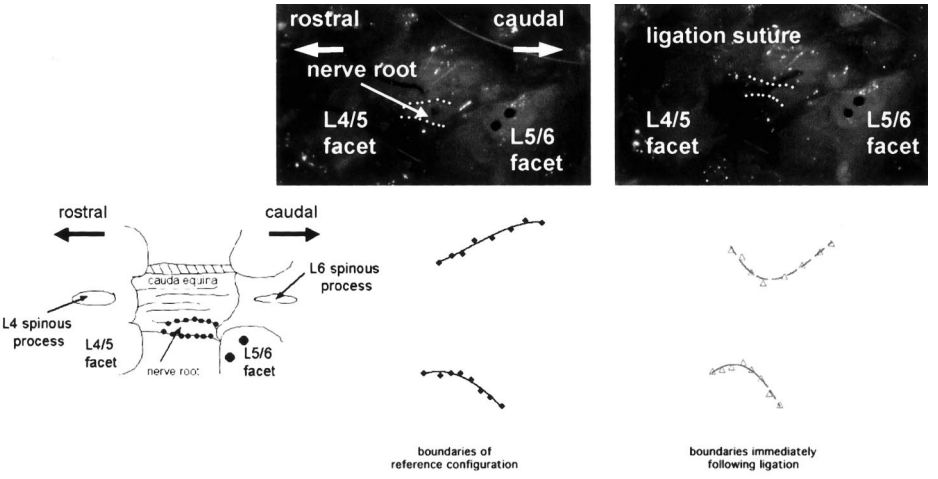

Figure 1. The diagram on the left schematically illustrates the L5 laminectomy exposing the cauda equina and L5 nerve root. The nerve root border has been digitized (small black dots). The upper set of *in vivo* images on the right shows the initial unligated (reference) configuration (left) and the nerve root immediately after ligation (right). Superimposed on each image is the set of digitized boundary points along the nerve root (white dots) and the bony positional markers (black dots). The corresponding curve fits for the digitized nerve root boundaries also are shown in the lower set of images on the right.

Although it is implied that neural tissue damage results from endoneurial pressure, tissue loading has been related to edema formation only, and its effect on other physiologic aspects of pain has not been addressed as of this writing. Despite limited efforts to relate mechanical injury to physiology, the simultaneous correlation of local tissue mechanics with an associated overall pain response suggesting lumbar radiculopathy currently is absent in the literature.

Currently radiculopathy models are used to investigate pain mechanisms, involvement of the central nervous system, role of the immune system, and effect of chemical irritants with respect to radicular pain.[1,9,13,24] In these models, a compressive injury to lumbar nerve roots *via* ligation has been shown to produce consistent and predictable behaviors associated with radicular pain states. After mechanical injury of the nerve root, animals exhibit mechanical allodynia (increased sensitivity to a non-noxious stimulus) in the ipsilateral hind paw.[9] Such behavior also is a typical clinical sign in patients with lumbar radiculopathy, as is a positive straight-leg-raising response, providing a gauge for nociceptive responses. For example, it has been shown that the magnitude of the behavioral response is altered by the application of a loose or tight ligation or the addition of chemically irritating suture material.[9] Although only qualitatively describing the injury magnitude, the work of Hashizume et al[9] suggests a role of mechanical injury in pain.

The purpose of this study, therefore, was to quantify the relation between local mechanical injury to the nerve roots and a nociceptive behavioral response in the context of an existing lumbar radiculopathy animal model. The degree of mechanical injury imposed on lumbar nerve roots at the time of injury was quantified and related to behavioral responses, as measured by the degree of postoperative mechanical allodynia observed. Image analysis and strain calculation techniques are presented and discussed in the context of an existing *in vivo* pain model. Quantitative comparisons are made between the degree of mechanical allodynia and the magnitude of neural compression. These comparisons are discussed as relevant to lumbar radiculopathy.

■ Methods

Experiments were performed using male Holtzman rats, each weighing 225 to 350 g at the start of surgery. The animals were housed individually under United States Department of Agriculture- and Association for Assessment and Accreditation of Laboratory Animal Care-approved conditions with a 12- to 12-hour light–dark cycle and free access to food and water. All the experimental procedures were approved by the Dartmouth College Institutional Animal Care and Use Committee.

Surgical Protocol. All the surgical procedures were performed with the animals under inhalation anesthesia: 4% halothane for induction and 2% halothane for maintenance. This lumbar radiculopathy model used a previously developed and described surgical model.[9] Briefly, using an operating microscope (LFS 200; Carl Zeiss, Thornwood, NY), a left hemilaminectomy was performed at L5. Facetectomy of the left L5–L6 facet joints also was performed. At the time of surgery, the animals were divided into two groups: a sham group (n = 5) in which the left L5 dorsal and ventral roots were exposed only and a ligation group (n = 14) in which the L5 dorsal and ventral nerve roots were tightly ligated using a single 6-0 silk suture (Figure 1). After surgery, the wound was closed with silk suture and surgical staples, with the animals recovering in room air.

The surgical operating scope was equipped with a digital camera (Model DP10; Olympus Optical, Melville, NY), having a 1024 × 1280 pixel resolution, to image the surgical preparation and neural tissue *in vivo*. During surgery, a minimum of two marks were made on the exposed bony surfaces using acrylic black paint (Figure 1). Preliminary studies had determined that the paint had no deleterious effects *in vivo*. The bony markers provided positional data defining a local origin and orientation for each image of an animal's surgical exposure. Geometric calibration for each image eliminated magnification issues. For each surgery, images of the initial undeformed nerve root tissue configuration and the immediate postligation deformed configuration of the nerve root structure were acquired (Figure 1). For sham procedures, the nerve root exposure simply was reimaged for the deformed configuration images.

After surgery, the animals were followed for 7 days. When the animals were killed, the wound was reopened and the exposure area cleared of tissue regrowth. The wound area was

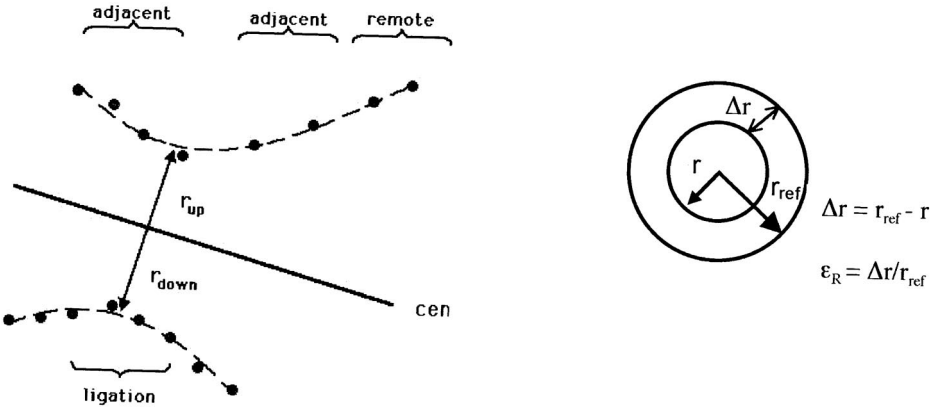

Figure 2. The schematic on the left illustrates the geometric definitions for calculating radial strains along the nerve root. The three anatomic regions also are labeled and defined on the basis of their locations relative to the ligation site (ligation, adjacent, remote). The drawing on the right is a schematic illustrating the nerve root in axial cross section, and defines the dimensions used for radial strain calculations (r = radius; cen = centerline).

imaged again to measure a postsurgical deformed tissue configuration.

Behavior Testing. The degree of mechanical allodynia in the ipsilateral hind paw of each animal was monitored on days 1, 3, 5, and 7 after surgery. Mechanical allodynia was measured as the number of hind paw withdrawals elicited by a defined non-noxious mechanical stimulus.[3] This technique is a common method for quantifying mechanical allodynia in rodent models.[1,3,9,10] The animals were acclimated previously to the testing environment and the tester. Baseline measurements were determined for each animal before the initial surgical procedure. All behavior testing was performed by the same tester.

In each testing session, the rats were subjected to three rounds of 10 tactile stimulations to the plantar surface of the hind paw using 2- and 12-g von Frey filaments (Stoelting, Wood Dale, IL). These von Frey filaments are monofilament fibers approximately 3.8 cm long. When pressed at right angles to the skin surface, the filaments bend at a given applied force, in this case at either 2 or 12 g. For the behavior assessments used in this study and others, such pressure on the hind paw normally elicits no response from the animals. However, after surgery, the animals exhibit a paw withdrawal reflex when touched with the filament.

Image and Strain Analysis. Using the bony marker locations and calibration images, each set of images for a given animal was transformed into the coordinate system defined by the initial reference image, allowing comparative geometric measurements to be made immediately after injury and after surgery. Locations of the bony landmarks were digitized using ImageTool Software (UTHSCSA, San Antonio, TX). Point locations and the orientation of the line defined by their endpoints were used to transform image orientations to that of the reference coordinate system. The boundary of the nerve root also was digitized along the outermost edges of its structure for each image set (Figures 1 and 2), providing a set of contours describing the "face-on" view of the nerve root in its *in vivo* unligated, immediately ligated, and postsurgical ligated geometries. For sham surgeries, the sets of contours consisted of unligated and postsurgical unligated geometries.

Cubic polynomials were used to provide close fits for the digitized boundary points of each specimen for each of its loading scenarios (Figure 2). Three regions along the nerve root structure were defined as the area of the ligation, directly adjacent to this site and more remote from the ligation (Figure 2). Such regional divisions allowed assessment of any anatomic variation in strain over the postsurgical follow-up period. For purposes of evaluating radial strain, the nerve root was approximated as a cylinder having a circular cross section with a variable diameter along its length. Under such an assumption, the diameter of the circular cross section was calculated by determining the difference between the two contours in the radial direction (Figure 2). Customized Fortran code was used to determine the center line and corresponding radius from each set of boundaries. Radial strain (ϵ_R) was calculated along the length for the exposed nerve root using the initial unligated (r_{ref}) measurements as a reference,[7] where

$$\varepsilon_R = \frac{r - r_{ref}}{r_{ref}} \quad (1)$$

This calculation was performed along the nerve root for initial ligation and on postsurgical day 7. Radial strain was calculated also for the sham surgery cases. To assess the utility of this *in vivo* strain method, error quantification was performed to calculate the error in imaging, digitization, curve fitting, and strain analysis for the ligation and sham approaches.

Statistical Analysis. All the data obtained from the observations of mechanical allodynia were combined as the mean response of the animals in each procedural group. The ligation animals were further divided into two groups according to the magnitude of the initial injury, and a Student *t* test was used to compare these differences in strain for the two groups. To compare the time-dependent curves between strain groups, a repeated analysis of variance was used. Significance was defined at a level of 0.05 or less.

■ Results

All the animals of the ligation group exhibited mechanical allodynia after nerve root injury. Initially, a robust allodynic response was observed, followed by a gradual decrease in response magnitude for both the 2- and 12-g von Frey filaments (Figures 3A and 3B). Allodynic responses for the ligation animal group were significantly elevated over the corresponding baseline responses for these animals ($P < 0.001$), and significantly greater than the responses for the animals undergoing sham surgery ($P = 0.001$). This was the case for both von Frey filament intensities. Moreover, the postsurgical behavioral response values of the sham animals were not different from their corresponding baseline values.

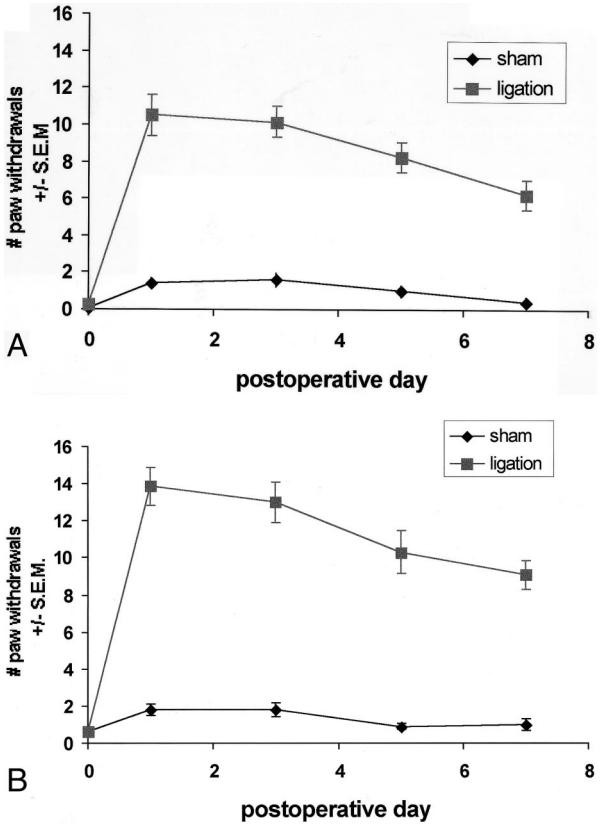

Figure 3. Mean mechanical sensitivity for the sham and ligation groups of animals. Foot-lift response frequency to stimulation with 2- and 12-g von Frey filament is depicted over the 7 days of the study. There was a significant increase in mean mechanical allodynia ($P = 0.001$) for testing using both 2-g (**A**) and 12-g (**B**) von Frey filaments for the ligation animals, as compared with the sham animals. The total number of responses resulting from 30 stimulations per animal was recorded, and the group average and standard error are reported.

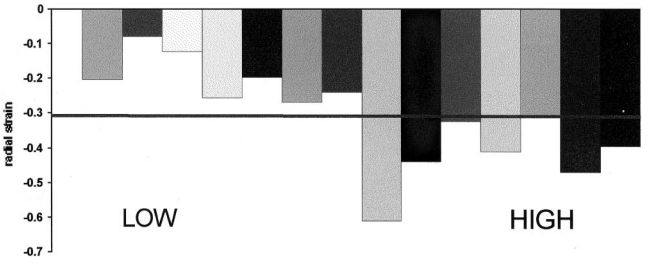

Figure 4. The ligation strain was compressive (negative) in all the animals tested. There was a high degree of variability in applied strain despite the surgeon's efforts to impose a tight ligation. The mean of all the ligations was 30.8% ± 14.5%, as indicated on the graph. The animals were grouped according to their strain magnitudes as belonging to either a high- or low-strain group.

The errors associated with the digitization methods and radial strain approximation techniques used in this study were small relative to imposed compressive strain magnitudes. The mean errors in estimating the *in vivo* radial strains were 0.5% ± 0.3% and 0.9% ± 0.9% along the nerve root for the sham and ligation surgeries, respectively. For the animals undergoing sham surgeries, with only nerve root exposure, the mean magnitude of radial strain was 1.04% ± 1% (range, −2.7–1.7%).

For an applied nerve root ligation, the measured radial strains were compressive and highly variable, ranging in magnitude from 7.8% to 61% (mean, 30.8% ± 14.5%) (Figure 4). This variability occurred despite the surgeon's best effort to impose consistently "tight" ligations. Not surprisingly, the degree of compression was found to decrease remote to the site of direct ligation: 26.5% ± 14.5% in the region adjacent to the ligation and 15.8% ± 18.7% in the region more remote from the injury.

On the basis of the large variation observed for the imposed ligation strain, two strain groups were created to delineate the effect of ligation magnitude on behavioral responses. A high-strain group (n = 7) comprised the animals undergoing ligations greater than the mean strain of all the ligation animals, and a low-strain group (n = 7) comprised animals undergoing strains less the overall mean (Figure 4). Using a Student *t* test, the two groups were determined to be significantly different in strain magnitude ($P = 0.0002$). The mean compressive strain was 42.3% ± 10% for the high-strain group and 19.4% ± 7.1% for the low-strain group. Grouping of the behavioral response data accordingly showed a relation between the intensity of ligation compression and the magnitude of mechanical allodynia observed (Figures 5A and 5B). For both the 2- and 12-g von Frey filaments, the high-strain group consistently exhibited a higher pain response than the lower strain group, as measured by mechanical allodynia. Overall, the behavioral responses between the strain groups were not significantly different for the 2-g testing despite an obvious trend (Figure 5A). However, for the 12-g von Frey filament, the overall behavioral response of the high-strain group was greater than that of the low strain group ($P = 0.05$) (Figure 5B).

A high degree of postoperative variation was observed along the nerve root on postoperative day 7. Postsurgically, regardless of imposed ligation magnitude or regional position relative to the ligation site, the nerve root underwent a tensile strain or swelling relative to its ligated configuration (Figure 6). The degree of swelling was more uniform across anatomic regions in the low-strain group than in the high-strain group. Yet the postoperative structural changes did not differ significantly for group or region.

■ Discussion

Clinical findings imply that mechanical deformation (*e.g.*, from disc herniation or lateral recessed stenosis) *via* impingement of the lumbar nerve root likely plays a role in the mechanism of radiculopathy.[11,18,25] However, the specific nature of the relation to pain remains unclear. For example, patients with similar degrees of disc herniation and nerve root impingement may exhibit widely varying pain states. Although the use of mechanical injuries as imposed injuries to the nerve roots and spinal nerves has been the basis for animal models of lumbar

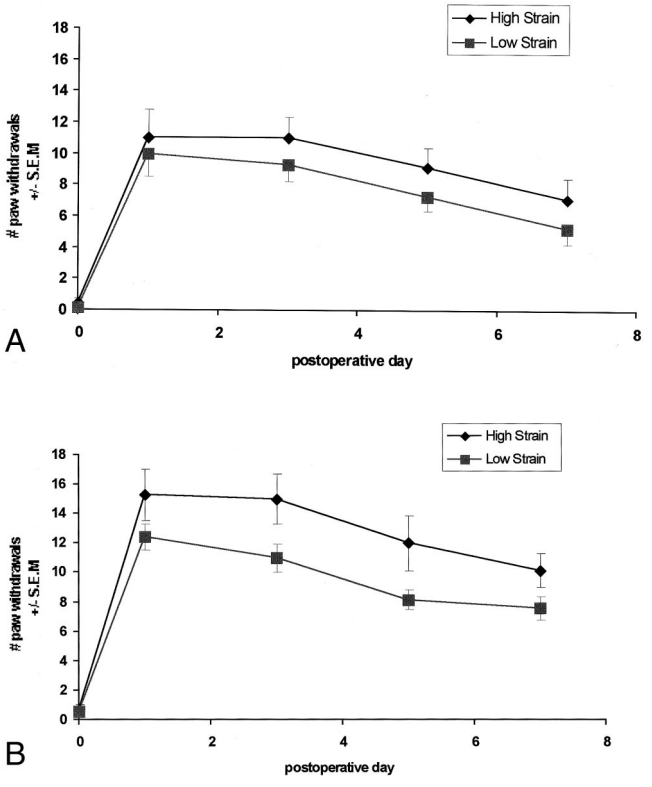

Figure 5. Mechanical sensitivity is shown for the ligation group of animals divided according to the magnitude of imposed ligation strains. For stimulations using both 2- (**A**) and (**B**) 12-g von Frey filaments, the high-strain group exhibited increased mechanical allodynia, as compared with the low-strain group. This was significant ($P = 0.05$) for the 12-g testing (**B**), and suggests a direct relation between tissue deformation and mechanical sensitivity after ligation injury.

radiculopathy and neuropathic pain,[1,9,13,24] quantitative assessment of the injury severity has not been performed. To the authors' knowledge, this study is the first to provide a quantitative characterization of local *in vivo* nerve root deformations, and to link these measurements with a resulting radicular nociceptive behavioral response typically observed in humans.

The behavioral responses observed for this injury model are consistent with those previously reported after use of a single silk ligation.[9] Moreover, postoperative behavioral data indicate that there is indeed a relation between deformation magnitude and measured mechanical allodynia. The animals experiencing larger compressive strains during ligation displayed more severe nociceptive responses (Figures 5A and 5B). Most simply, this means that the greater the compression, the worse the clinical symptoms, as measured by mechanical allodynia. Although this relation was implied in previous work using loose and tight ligations to produce behavioral responses of differing intensities,[9] the simultaneous quantitative characterization of the initial injury had not been performed before the implementation of this *in vivo* technique.

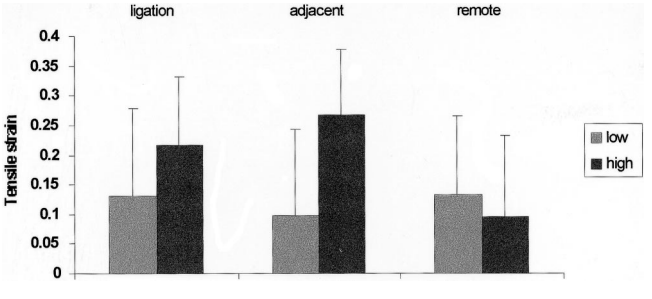

Figure 6. After surgery, the mean strains in each anatomic region were tensile (positive) in nature, which suggests tissue swelling. This was the case along the nerve root and in both strain groups. No significant differences in the degree of swelling were found in comparisons by region or by ligation strain magnitude.

Less clear were the radial changes observed to occur after surgery. The mean radial changes in the nerve root were all positive- and suggestive of swelling along the nerve root after ligation (Figure 6). Indeed, tissue edema has been produced after mechanical compression of the lumbar nerve roots and nerves.[14,19,22] It is difficult to compare the existence of tissue swelling in the current study with that reported by others because previous studies have not reported any uninjured data for reference and quantitative comparison. The large degree of variation anatomically and with respect to injury strain also suggests that the structural tissue response may be quite different for different individuals. Such a finding may explain, in part, the large degree of variation observed clinically in patients exhibiting disc herniation or spinal stenosis and varying degrees of pain or, alternatively, pain in the absence of a presenting disc herniation or stenosis.

Moreover, the postoperative tissue configuration data (Figure 6) further suggest that the degree of swelling along the nerve root length was more uniform among the looser ligations than in the high-strain group. These regional changes may provide one mechanism through which the nociceptive response is generated and graded for injury intensity. Perhaps the looser ligations do not generate a profound cascade of physiologic events either locally or centrally (downstream). In turn, this diminished response may not produce as strong a structural reaction locally or as intense a behavioral response as may occur in a more severe injury. However, it should be noted that currently, only the local structural changes and behavioral data have been investigated after surgery.

It is possible that, depending on the severity of the initial mechanical injury, different neuroinflammatory changes in the central nervous system may be responsible for eliciting the graded responses observed for the different strain groups (Figures 5A and 5B). The authors currently are investigating the role of central neuroinflammation in the etiology of lumbar radiculopathy.[1,3,9,10] They also are characterizing these changes in terms of injury intensity. The postsurgical local tissue changes may be caused by a variety of other factors brought into play after the initial injury, and thus may not provide a direct correlation with the observed behavioral responses.

It should be noted also that the postoperative time point of day 7, selected on the basis of previous studies

using this model,[1,9,10] provides only a snapshot of the local tissue changes. The corresponding behavioral data at this time point indicate that mechanical allodynia has not resolved. Therefore, the postoperative mechanical data likely reflect the highly complicated mechanical environment, which itself results from both mechanical and physiologic actions. Notably, local swelling after injury may not contribute to behavioral sensitivity as much as the local tissue damage intensity at the time of injury does. Clinically, patients experience various symptoms during various periods, despite a "successful" surgical procedure.

Use of the techniques presented for *in vivo* biomechanical analysis required a number of simple assumptions. These included using a two-dimensional image of the nerve root exposure. Although it provides a pragmatic representation of geometric changes *in vivo*, this approximation does not consider any local variation in nerve root geometry that may occur out of the plane of imaging. Moreover, the cross section of the nerve root geometry has been approximated as a circle, further implying that any geometric changes in the radial direction are uniform around a center. However, the current study offered, for the first time, local *in vivo* measurements at the site of injury in a radiculopathy model. For this reason, it provides both the orthopedic–neurosurgical and engineering communities with highly relevant data linking local biomechanics with a pain response.

Future studies are needed for a full delineation of the relation between local biomechanics and the specific physiologic pathways involved with pain onset and persistence, but the current results indicate that the degree of initial mechanical injury likely plays an important role in the cascade of events that follow. Although the local anatomic structure may not be largely different after the injury, the current findings suggest that perhaps there exists a threshold for initial mechanical deformation in the nerve root that elicits varying pain responses. Moreover, these results highlight the need for continued work to decipher the specific role of mechanical deformation in lumbar radiculopathy and its relation to the other physiologic factors involved, including electrophysiologic changes, neuroinflammatory changes, and local edema.

■ Key Points

- Biomechanical techniques can be applied to an animal model of lumbar radiculopathy, then used to show that mechanical injury (deformation) of the lumbar nerve root has a role in radicular pain.
- The degree of ipsilateral mechanical allodynia partly depends on the severity of the local mechanical injury, as measured by the magnitude of radial strain applied to the nerve root.
- Structural and anatomic changes in the nerve root manifested after surgery suggest swelling and are highly variable.

References

1. Colburn R, Rickman A, DeLeo J. The effect of site and type of nerve injury on spinal glial activation and neuropathic pain behavior. Exp Neurol 1999;157: 289–304.
2. Cornefjord M, Sato K, Olmarker K, et al. A model for chronic nerve root compression studies: Presentation of a porcine model for controlled slow-onset compression with analyses of anatomic aspects, compression onset rate, and morphologic and neurophysiologic effects. Spine 1997;22: 946–57.
3. DeLeo JA, Colburn RW. The role of cytokines in nociception and chronic pain. In: Weinstein JN, Gordon SL, eds. Low Back Pain: A Scientific and Clinical Overview. Rosemont, IL: AAOS Publishers, 1996:163–85.
4. Deyo RA, Tsui-Wu YJ. Descriptive epidemiology of low back pain and its related medical care in the United States. Spine 1987;12:264–8.
5. Frymoyer J, Cats-Baril W. An overview of the incidences and costs of low back pain. Orthop Clin North Am 1991;22:263–71.
6. Frymoyer J, Durett C. The economics of spinal disorders. In: Frymoyer JW, ed. The Adult Spine: Principles and Practice. Philadelphia: Lippincott-Raven Publishers, 1999.
7. Fung YC. Foundations of Solid Mechanics. Englewood Cliffs, NJ: Prentice-Hall, 1965.
8. Hanai F, Matsui N, Hongo N. Changes in responses of wide dynamic range neurons in the spinal dorsal horn after dorsal root or dorsal root ganglion compression. Spine 1996;21:1408–15.
9. Hashizume H, DeLeo JA, Colburn RW, et al. Spinal glial activation and cytokine expression after lumbar root injury in the rat. Spine 2000;25:1206–17.
10. Hashizume H, Rutkowski, MD, Weinstein JN, et al. Central administration of methotrexate reduces mechanical allodynia in an animal model of radiculopathy/sciatica. Pain 2000;87:159–69.
11. Hollingworth W, Dixon AK, Todd CJ, et al. Self-reported health status and magnetic resonance imaging findings in patients with low back pain. Eur Spine J 1998;7:369–75.
12. Hu S, Xing J. An experimental model for chronic compression of dorsal root ganglion produced by intervertebral foramen stenosis in the rat. Pain 1998; 77:15–23.
13. Kawakami M, Weinstein JN, Chatani K, et al. Experimental lumbar radiculopathy: Behavioral and histologic changes in a model of radicular pain after spinal nerve root irritation with chromic gut ligatures in the rat. Spine 1994;19:1795–802.
14. Lundborg G, Myers R, Powell H. Nerve compression injury and increased endoneurial fluid pressure: A "miniature compartment syndrome." J Neurol Neurosurg Psych 1983;46:1119–24.
15. Mao G, Konno S, Arai I, et al. Chronic double-level cauda equina with analyses of nerve conduction velocity. Spine 1998;23:1641–4.
16. Matsui H, Maeda A, Tsuji H, et al. Risk indicators of low back pain among workers in Japan: Association of familial and physical factors with low back pain. Spine 1997;22:1242–7.
17. Olmarker K, Holm S, Rydevik B. Importance of compression onset rate for the degree of impairment of impulse propagation in experimental compression injury of the porcine cauda equina. Spine 1990;15:416–19.
18. Olmarker K, Myers RR. Pathogenesis of sciatic pain: Role of herniated nucleus pulposus and deformation of spinal nerve root and dorsal root ganglion. Pain 1998;78:99–105.
19. Olmarker K, Rydevik B, Holm S. Edema formation in spinal nerve roots induced by experimental, graded compression: An experimental study on the pig cauda equina with special reference to differences in effects between rapid and slow onset of compression. Spine 1989;14:569–73.
20. Pedowitz R, Garfin S, Massie J, et al. Effects of magnitude and duration of compression on spinal nerve root conduction. Spine 1992;17:194–9.
21. Rydevik B, Hasue M, Wehling P. Etiology of sciatic pain and mechanisms of nerve root compression. In: Wiesel SW, Weinstein JN, Herkowitz H, et al, eds. The Lumbar Spine. Philadelphia: WB Saunders, 1996:123–41.
22. Rydevik B, Myers R, Powell H. Pressure increase in the dorsal root ganglion following mechanical compression: Closed compartment syndrome in nerve roots. Spine 1989;14:574–6.
23. Skouen J, Brisby H, Otami K, et al. Protein markers in cerebrospinal fluid experimental nerve root injury: A study of slow-onset chronic compression effects or the biochemical effects of nucleus pulposus on sacral nerve roots. Spine 1999;24:2195–200.
24. Song X, Hu S, Greenquist K, et al. Mechanical and thermal hyperalgesia and ectopic neuronal discharge after chronic compression of dorsal root ganglia. J Neurophysiol 1999;82:3347–58.

25. Vucetic N, Astrand P, Guntner P, et al. Diagnosis and prognosis in lumbar disc herniation. Clin Orthop 1999;361:116–22.
26. Wall P, Melzack R, eds. Textbook of Pain, 3rd ed. London: Churchill Livingstone, 1994.
27. Weinstein J, Gordon S, eds. Low Back Pain: A Scientific and Clinical Overview. Rosemont, IL: American Academy of Orthopaedic Surgeons, 1996.
28. Yamaguchi K, Murakami M, Takahashi K, et al. Behavioral and morphological studies of the chronically compressed cauda equina: Experimental model of lumbar spinal stenosis in the rat. Spine 1999;24:845–51.
29. Yoshizawa H, Kobayashi S, Kubota K. Effects of compression on intraradicular blood flow in dogs. Spine 1989;14:1220–5.

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