Perfusion of the Mechanically Compressed Lumbar Ganglion With Lidocaine Reduces Mechanical Hyperalgesia and Allodynia in the Rat

JUN-MING ZHANG, HUIQING LI, AND SORIN J. BRULL
Department of Anesthesiology, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205

Received 14 February 2000; accepted in final form 4 May 2000

Zhang, Jun-Ming, Huiqing Li, and Sorin J. Brull. Perfusion of the mechanically compressed lumbar ganglion with lidocaine reduces mechanical hyperalgesia and allodynia in the rat. J Neurophysiol 84: 798–805, 2000. The rat L5 dorsal root ganglion (DRG) was chronically compressed by inserting a hollow perforated rod into the intervertebral foramen. The DRG was constantly perfused through the hollow rod with either lidocaine or normal saline delivered by a subcutaneous osmotic pump. Behavioral evidence for neuropathic pain after DRG compression involved measuring the incidence of hindlimb withdrawals to both punctate indentations of the hind paw with mechanical probes exerting different bending forces (hyperalgesia) and to light stroking of the hind paw with a cotton wisp (tactile allodynia). Behavioral results showed that for saline-treated control rats: the withdrawal thresholds for the ipsilateral and contralateral hind paws to mechanical stimuli decreased significantly after surgery and the incidence of foot withdrawal to light stroking significantly increased on both ipsilateral and contralateral hind paws. Local perfusion of the compressed DRG with 2% lidocaine for 7 days at a low flow-rate (1 μl/h), or for 1 day at a high flow-rate (8 μl/h) partially reduced the decrease in the withdrawal thresholds on the ipsilateral foot but did not affect the contralateral foot. The incidence of foot withdrawal in response to light stroking with a cotton wisp decreased significantly on the ipsilateral foot and was completely abolished on the contralateral foot in the lidocaine treatment groups. This study demonstrated that compression of the L5 DRG induced a central pain syndrome that included bilateral mechanical hyperalgesia and tactile allodynia. Results also suggest that a lidocaine block, or a reduction in abnormal activity from the compressed ganglia to the spinal cord, could partially reduce mechanical hyperalgesia and tactile allodynia.

INTRODUCTION

Animal models of neuropathic pain are supported with behavioral evidence of spontaneous pain and cutaneous hyperalgesia after injury of peripheral nerves (Bennett and Xie 1988; Kim and Chung 1992; Seltzer et al. 1990) or dorsal root ganglia (DRG) (Hu and Xing 1998; Olmarker and Myers 1998; Song et al. 1999). Although the mechanism of neuropathic pain following nerve/ganglion injury is unresolved, evidence suggests that somata of the DRG may become an important source of pain after an injury of the peripheral nerve (Devor and Obermayer 1984). When rat peripheral nerves or primary sensory neurons are injured, certain DRG neurons become hyperexcitable and may exhibit various patterns of abnormal ectopic discharge (Babbedge et al. 1996; Burchiel 1984; Hu and Xing 1998; Kajander et al. 1992; Wall and Devor 1983; Xie et al. 1995; Zhang et al. 1997b, 1999). The ionic and cellular mechanisms of the increased excitability are not known, but accumulation of certain types of sodium channels at the injured site or the related DRGs may account for the changes in membrane properties of the DRG somata and thus contribute to the enhancement of neuronal excitability (Devor et al. 1993; Rizzo et al. 1993; Zhang et al. 1997a).

Evidence that modulation of sodium currents in the DRG may alter neuropathic pain comes from neuropathic animal models where systemic administration of lidocaine suppressed the ectopic discharges recorded extracellularly in the neuroma, the DRG, or the spinal horn neurons (Chabal et al. 1989; Devor et al. 1992; Omana-Zapata et al. 1997b; Sotgiu et al. 1992). Systemic lidocaine treatment also prevented the development of thermal hyperalgesia and cutaneous thermal abnormalities after peripheral nerve injury in rats (Sotgiu et al. 1995). It is not known, however, to what extent the alteration in neuronal excitability and abnormal activities originating in the DRG contribute to the development of pain and hyperalgesia.

In the present study, we investigated the neurological mechanisms of cutaneous hyperalgesia and tactile allodynia using an animal model of lumbar radiculopathy. In this model, a stainless steel, hollow, perforated rod was inserted surgically into the intervertebral foramen to produce a chronic compression of the L5 DRG. The procedure was similar to the model described elsewhere (Hu and Xing 1998; Song et al. 1999) except that the inserted solid rod used previously was replaced by a hollow rod connected to an osmotic pump and that only one, not two DRGs, was chronically compressed. The justification for this new animal model is that clinically, single-ganglion compression/injury is more common than two-ganglion-compression injuries. The purposes of this study were to evaluate whether mechanical hyperalgesia and allodynia were present after a chronic compression of the L5 DRG and to measure the changes in cutaneous sensitivity after blocking/reducing the input of abnormal activity from the compressed ganglion to the spinal horn by delivering different rates of lidocaine to the compressed ganglion in vivo.

METHODS

Fifty-seven adult, male, Sprague-Dawley rats were used for all the experiments. At the start of experiment the animal weights were between 150 and 200 g. Animals were housed in groups (3 per cage)
The tube leading from the pump was filled with 10% lidocaine or normal saline according to the methods described elsewhere (Munson et al. 1997; Oyelese et al. 1997; Verge et al. 1995). Lidocaine or normal saline by an investigator other than the one performing behavioral testing to avoid possible introduction of testing bias. At the end of each experiment, the ganglion was carefully examined under a dissecting microscope. The appearance of the dye in or around the ganglion was considered an indication that the delivered drug reached the compressed ganglion.

**Behavioral testing procedures**

Animals were inspected and tested every day for 3 days prior to surgery, every other day for the first two postoperative weeks, twice during the 3rd week, and once last time at the end of 4 wk postoperatively for a total of 13 testing sessions. The testing procedure was described previously (Song et al. 1999). Briefly, the rat was acclimated, prior to the test, for 15 min and tested in a closed Plexiglass box with a mesh floor (with $1 \times 1$ cm openings) through which mechanical stimuli were applied.

**WITHDRAWAL TO PUNCTATE MECHANICAL STIMULATION OF THE FOOT.** Mechanical probes consisting of nylon filaments that had bending forces of 5, 10, 20, 40, 60, 80, 100, 120, and 160 mN, and 100-μm cylindrical tips were applied to the plantar surface of the foot from underneath the cage floor. Each filament was applied once to 10 different predetermined locations on the ventral surface, spaced across nearly the entire extent of the paw. The duration of each stimulus was 1 s and the interstimulus interval was 10–15 s. The mechanical probes were applied in the order of increasing bending force, with a given filament delivered to each spot alternatively from one paw to the other in sequence (from the first to the tenth spot) until a 100% response to certain force was evoked on both paws. The modified filaments differed in some respects from the conventional von Frey filaments used to measure withdrawal thresholds to mechanical stimulation of the rat hind paw. The bending force of the modified filaments was independent of the filament diameter. The diameter of the tip was held constant by attaching 100-μm-diam rods to nylon filaments of differing diameter to deliver a “blunt pinprick” to the ventral surface of the hind paw. The advantage of this method was that preoperative thresholds were easily obtained without the need for thicker filaments with blunt tip diameters that could sometimes lift the paw under pressure without eliciting a withdrawal response.

**Calculation of the withdrawal thresholds to mechanical stimulation.** Since the percent withdrawal responses plotted as a function of the stimulus magnitudes (bending forces) were hyperbolic, but not linear, the Hill equation, $P = P_{\text{max}} S^g/(S_{50} + S^g)$, which provided the best nonlinear least square curve-fit to the data, was used to estimate the $S_{50}$ and the slope factor ($g$). The parameters in the equation represent percent response ($P$), the maximal response or 100% withdrawal response ($P_{\text{max}}$), the stimulus magnitude ($S$), the stimulus magnitude or the force associated with 50% response of foot withdrawal ($S_{50}$), and a slope factor ($g$), known as the Hill coefficient. Fitting the data to the Hill equation was done using a curve-fitting program (Microcal Origin 5.0, Microcal Software, Northampton, MA).

**FOOT WITHDRAWAL TO INOCUOUS MECHANICAL STIMULI.** A wisp of cotton pulled up but still attached to a cotton swab was stroked mediolaterally across the plantar surface of the skin through the floor of the plastic cage. Six strokes were delivered to each foot, alternating between right and left with each stroke. The duration of each stroke was 1 s, and the inter-stroking interval was 10–15 s. A single, quick withdrawal reflex was considered to indicate the presence of tactile allodynia.

**Statistical analysis**

Data were expressed as means and standard errors of the mean (SE). Differences in withdrawal thresholds over time were tested using Friedman repeated-measures ANOVA on Ranks followed by
Mechanical hyperalgesia in L5 DRG-compressed rats

In 13 rats, the L5 DRG was compressed with a 0.7-mm rod and perfused with normal saline at a low flow-rate (1 μl/h) for the first postoperative week. Figure 2 shows results for 3 days before and 1, 7, 14, 21, and 28 days after compression of the DRG (n = 13, low flow-rate saline group). A: ipsilateral to the injury; B: contralateral to the injury. Note that the force-response curve shifted leftward on both hind paws after surgery suggesting a decreased withdrawal threshold.

Post hoc pairwise comparisons. Difference in withdrawal thresholds between presurgery and a specific day postsurgery was tested using Wilcoxon signed-rank test. Two-way ANOVA involving the factors treatment (saline, lidocaine) and postoperative day was used to test the significance of differences in withdrawal thresholds between experimental conditions. A probability of 0.05 was chosen as the criterion for significance. The Bonferroni method was used when necessary to correct the probability level for multiple comparisons.

RESULTS

In general, all rats appeared in good health throughout the testing period. They gained weight and exhibited no self-inflicted wounds. The level of general activity was normal during the testing period after surgery.

Mechanical hyperalgesia in L5 DRG-compressed rats

In 13 rats, the L5 DRG was compressed with a 0.7-mm rod and perfused with normal saline at a low flow-rate (1 μl/h) for the first postoperative week. Figure 2 shows results for 3 days before and 1, 7, 14, 21, and 28 days after compression of the DRG (n = 13, low flow-rate saline group). A: ipsilateral to the injury; B: contralateral to the injury. Note that the force-response curve shifted leftward on both hind paws after surgery suggesting a decreased withdrawal threshold.

Mechanical hyperalgesia was at its maximum during the 2nd postoperative week (postoperative day 13) for both hind paws, at which time withdrawal thresholds decreased 40% for the contralateral (56.4 ± 2.2 vs. 33.6 ± 2.2 mN), and 65% for the ipsilateral foot (55.8 ± 2.0 vs. 19.4 ± 3.0 mN) from prelesion threshold. After postoperative day 15, thresholds recovered slightly yet never returned to prelesion levels. Reduction in the withdrawal thresholds was greater on the ipsilateral foot suggesting a decreased withdrawal threshold.

The contralateral hind paw on the first postoperative day exhibited a significantly decreased sensitivity to mechanical stimuli (hypoalgesia) in 6 of 13 rats tested (before surgery: 57.3 ± 4.2 mN; postoperative day 1: 71.2 ± 6.3 mN; P < 0.05, Wilcoxon signed-rank test). This hypoalgesia disappeared in all rats by day 3 after surgery. Despite the initial hypoalgesia, the withdrawal threshold on the contralateral foot decreased significantly from 56.4 ± 2.2 mN before surgery, to 45.5 ± 3.6 mN on the 3rd postoperative day (P < 0.05, Wilcoxon signed-rank test). The decreased withdrawal threshold on the contralateral foot lasted for more than 4 wk after surgery (P < 0.05, Friedman repeated-measures ANOVA on ranks; Fig. 3A).

Mechanical hyperalgesia was at its maximum during the 2nd postoperative week (postoperative day 13) for both hind paws, at which time withdrawal thresholds decreased 40% for the contralateral (56.4 ± 2.2 vs. 33.6 ± 2.2 mN), and 65% for the ipsilateral foot (55.8 ± 2.0 vs. 19.4 ± 3.0 mN) from prelesion threshold. After postoperative day 15, thresholds recovered slightly yet never returned to prelesion levels. Reduction in the withdrawal thresholds was greater on the ipsilateral foot suggesting a decreased withdrawal threshold.

The withdrawal thresholds obtained from the $S_{50}$ using the Hill equation for all 13 rats markedly decreased after DRG compression. Preoperative withdrawal threshold on the ipsilateral hind paw, averaged for the 3 days of testing, was 55.8 ± 2.0 mN; this threshold decreased significantly to 33.8 ± 3.6 mN on the first postoperative day (P < 0.05, Wilcoxon signed-rank test). Postoperative threshold was lower than preoperative threshold for the entire postoperative testing period of 28 days (P < 0.05, Friedman repeated measures ANOVA on ranks; Fig. 3A).

The contralateral hind paw on the first postoperative day exhibited a significantly decreased sensitivity to mechanical stimuli (hypoalgesia) in 6 of 13 rats tested (before surgery: 57.3 ± 4.2 mN; postoperative day 1: 71.2 ± 6.3 mN; P < 0.05, Wilcoxon signed-rank test, n = 6). This hypoalgesia disappeared in all rats by day 3 after surgery. Despite the initial hypoalgesia, the withdrawal threshold on the contralateral foot decreased significantly from 56.4 ± 2.2 mN before surgery, to 45.5 ± 3.6 mN on the 3rd postoperative day (P < 0.05, Wilcoxon signed-rank test). The decreased withdrawal threshold on the contralateral foot lasted for more than 4 wk after surgery (P < 0.05, Friedman repeated-measures ANOVA on ranks; Fig. 3A).

Mechanical hyperalgesia was at its maximum during the 2nd postoperative week (postoperative day 13) for both hind paws, at which time withdrawal thresholds decreased 40% for the contralateral (56.4 ± 2.2 vs. 33.6 ± 2.2 mN), and 65% for the ipsilateral foot (55.8 ± 2.0 vs. 19.4 ± 3.0 mN) from prelesion threshold. After postoperative day 15, thresholds recovered slightly yet never returned to prelesion levels. Reduction in the withdrawal thresholds was greater on the ipsilateral foot suggesting a decreased withdrawal threshold.

The withdrawal thresholds obtained from the $S_{50}$ using the Hill equation for all 13 rats markedly decreased after DRG compression. Preoperative withdrawal threshold on the ipsilateral hind paw, averaged for the 3 days of testing, was 55.8 ± 2.0 mN; this threshold decreased significantly to 33.8 ± 3.6 mN on the first postoperative day (P < 0.05, Wilcoxon signed-rank test). Postoperative threshold was lower than preoperative threshold for the entire postoperative testing period of 28 days (P < 0.05, Friedman repeated measures ANOVA on ranks; Fig. 3A).
Effects of local perfusion of the DRG with lidocaine on mechanical hyperalgesia

LOW PERFUSION RATE. In this series of experiments, 2% lidocaine was delivered to each compressed ganglion of 18 rats at a flow-rate of 1 μl/h for the first 7 postoperative days. In comparison with prelesion levels, withdrawal thresholds were significantly lower for the ipsilateral hind paw, between days 1 and 17 after DRG compression (P < 0.05, Friedman repeated-measures ANOVA on ranks) in the lidocaine-treated rats. After day 17, withdrawal thresholds to mechanical stimulation recovered toward baseline. For the contralateral hind paw, withdrawal thresholds decreased postoperatively, but to a lesser extent than that observed for the ipsilateral hind paw.

Compared with saline-treated rats, the withdrawal thresholds were significantly higher on the ipsilateral hind paw in lidocaine-treated rats throughout the testing period (P < 0.05, 2-way repeated-measures ANOVA; Fig. 4B). For the contralateral paw, lidocaine treatment did not affect the withdrawal thresholds during the first two postoperative weeks. The mechanical hyperalgesia returned toward to prelesion levels 17 days postoperatively; this was not observed in saline-treated rats, either ipsilaterally or contralaterally. By day 28, the withdrawal threshold on the contralateral foot was significantly higher in lidocaine-treated rats than in the saline-treated ones (P < 0.05, Wilcoxon signed-rank test). Moreover, contralateral hypoalgesia, as occurred in saline-treated rats during first postoperative day, was not observed in lidocaine-treated rats (Fig. 5B).

Tactile allodynia induced by DRG compression

Preoperatively, none of the 13 rats implanted with the low flow-rate saline pumps responded with quick foot withdrawals to any of the six strokes of a cotton wisp applied to either foot. As early as 1st day postoperatively, two rats exhibited tactile allodynia on the ipsilateral paw, but most rats developed quick responses to light strokes after day 5 that lasted throughout the period of testing (Fig. 5A). Additionally, saline-treated rats with L₅ DRG compression developed guarding behavior ipsilateral to the side of the surgery, such as avoidance of weight-bearing and occasionally holding the ipsilateral hind paw in the air in a protected position. The occurrence of licking of the ipsilateral hind paw also suggested the presence of spontaneous pain or allodynia.

Tactile allodynia was observed on the contralateral paw with a delayed onset and a lower incidence of foot withdrawal (Fig. 5A) that increased over time following surgery. In general, 90% of the rats exhibited a reflex withdrawal to the stroke of a cotton wisp applied to the foot ipsilateral to the compressed DRG. For the contralateral foot, 50% of the rats responded to the cotton wisp application during the period of postoperative testing.
This study demonstrated that compression of the L3 DRG induced a central pain syndrome that included bilateral mechanical hyperalgesia and tactile allodynia. Results also suggest that a lidocaine block or reduction of abnormal activity from the compressed ganglia to the spinal cord could prevent the development of mechanical hyperalgesia and allodynia.

The procedure used differs from the DRG compression models reported previously (Hu and Xing 1998) in three ways. First, L-shaped rods were used instead of straight ones to prevent the intrusion of the inserted rod into the spinal cord. Second, the solid rod was replaced with a hollow, perforated one. And third, the rod was connected to an implanted pump for the delivery of various chemicals to the compressed ganglion. This procedure also differs from the one reported previously, in which both L4 and L5 lumbar ganglia were compressed with 0.6-mm solid stainless steel rods (Song et al. 1999).

In the present study, we used the Hill equation, rather than the logit transformation as described in our previous studies (Song et al. 1999), to estimate the withdrawal thresholds in normal and DRG-compressed rat. The major reason for this change was that available methods used to estimate the withdrawal threshold, such as the up-down method (Chaplan et al. 1994), and the method we described previously (Song et al. 1999), were based on the assumption that the force-response curve was S-shaped. Thus a linear logistic transformation could be performed to calculate the 50% response force. However, we recently have found that compression of the L3 DRG with a 0.7-mm rod significantly increased mechanical sensitivity, such that in a small number of rats, a withdrawal response could be evoked by a force as low as 5 mN, the minimum force employed in our testing procedure. As a result, the force-response data resulted in a hyperbolic curve, instead of an S-shaped curve. Therefore logistic transformation would not precisely estimate the withdrawal threshold for such data. The Hill equation, however, provides ideal fitting for both S- and
hyperbolic shape response curves and was thus used to precisely estimate the withdrawal thresholds in both normal and neuropathic rats.

**MECHANICAL HYPERALGESIA.** Our behavioral results agree with those obtained from the two-ganglion compressed rat experiments, except that a significant decrease in the withdrawal threshold to mechanical stimuli was also observed on the contralateral hind paw. Thresholds in the contralateral hind paw were higher, and the onset of cutaneous hyperalgesia was slower than in the ipsilateral paw. Only occasionally in two-ganglion compressed rats was a change observed in withdrawal threshold on the contralateral foot (Zhang et al. 1999). In this study, because no surgery was performed on the contralateral side, the observed changes in withdrawal threshold on the contralateral foot were not likely related to the general surgical procedure. Contralateral hyperalgesia is not novel in animal neuropathic pain models, and it has been reported previously (Carlton et al. 1994; Kim and Chung 1992; Seltzer et al. 1990).

In some rats, the withdrawal threshold on the contralateral foot was significantly increased on the first postoperative day compared with the presurgical levels. We believe the contralateral hypoalgesia is surgery-related. After surgery, the ipsilateral limb may experience temporary weakness. Rats may tend to guard the injured side by shifting the whole body weight to the contralateral foot.

**TACTILE ALLODYNA.** Another significant finding of this study was that about 50% of rats with L5 DRG compression developed tactile allodynia on the contralateral hind paw: this has not been reported in any previous neuropathic animal model (Bennett and Xie 1988; Kim and Chung 1992; Seltzer et al. 1990). Compression of the L4 and L5 DRG with a solid rod of 0.6 mm in diameter failed to induce contralateral allodynia. Although the reason for this is not known, it is likely that development of contralateral hyperalgesia is related to the diameter of the rod that is used to compress the ganglion. A smaller diameter (e.g., 0.5-mm) rod tends to produce less mechanical hyperalgesia with no changes in the sensitivity on the contralateral hind paw (unpublished observation).

**MECHANISMS OF CUTANEOUS HYPERSENSITIVITY AFTER L5 DRG COMPRESSION.** It is believed that enhanced cutaneous sensitivity to noxious mechanical stimulation (tactile hyperalgesia) results from central sensitization of the spinal cord, which can develop in human subjects after receiving nociceptive inputs (C-fiber activity) for a period of time (Torebjork et al. 1992). In neuropathic animal models, abnormal nociceptive activity is generally thought to be generated at the injury site of the axons and more proximally from the DRG somata (Babbedge et al. 1996; Burchiel 1984; Czeh et al. 1977; Hu and Xing 1998; Kajander et al. 1992; Wall and Devor 1983; Xie et al. 1995; Zhang et al. 1997b). Spontaneous activity has been recorded from compressed, C-type DRG neurons (Zhang et al. 1999) and is believed to contribute to the development of mechanical hyperalgesia.

Aside from the C fibers, A fibers may also be involved in the development of painful behavior in CCD rats, especially tactile allodynia. It has been reported that Aβ fibers contribute to inflammatory hypersensitivity by switching their phenotype to one resembling pain fibers, thereby enhancing synaptic transmission in the spinal cord and exaggerating the central response to innocuous stimuli (Neumann et al. 1996). In CCD rats, an inflammatory reaction has been found in the ganglion (Zhang et al. 1999); therefore it is possible that a similar phenotypic switch may have occurred in Aβ-type CCD neurons. As a result, light stroking of the skin with a cotton wisp might evoke withdrawal responses in CCD rats because of recruitment of hyperexcitable Aβ neurons. Recently Porreca et al. (1999) reported an upregulation of PN3/SNS, a TTX-resistant sodium channel, in large, Aβ DRG neurons. Selective knock-down of this channel prevented tactile allodynia caused by peripheral nerve injury.

**LOCAL PERFUSION OF THE COMPRESSED DRG WITH LIDOCAINE.** Our results indicate that a short period of application of lidocaine locally to the compressed ganglion, and beginning at the time of surgery, partially prevented the development of mechanical hyperalgesia and significantly blocked tactile allodynia. These effects were present for a long postoperative period, and lasted well beyond the termination of lidocaine perfusion. Results from the present study are consistent with previous findings in rats with chronic constriction of the sciatic nerve in that lidocaine pretreatment of the injured nerve abolished paw licking reflex for a variable postoperative period (1 wk or more) and shortened the duration of thermal hyperalgesia. Our results also support the finding that a prolonged application of local anesthetics may prevent late development of cutaneous hyperalgesia as reported by Kissin et al. (1998).

It is likely that the recovery of mechanical hyperalgesia and tactile allodynia in lidocaine-treated rats resulted from the suppression of abnormal spontaneous activity. Previous electrophysiological studies have revealed that lidocaine abolished the spontaneous activity of A-type neurons/fibers when applied to the DRG or the injury site by inhibiting the Na+ channel activity (Chabal et al. 1989; Devor et al. 1992; Omama-Zapatka et al. 1997; Scholz et al. 1998; Sotgiu et al. 1991, 1995). We have determined, in previous studies, that the incidence of ectopic discharge in A-fibers obtained from two-ganglion-compressed rats was 8.6%, compared with 1% in control rats, and demonstrated that the discharge originated in the ganglion (Song et al. 1999). Although electrophysiological recordings were not performed in the present study, it is reasonable to suggest that lidocaine, when applied to the DRG, partially suppressed spontaneous activity, which may have delayed the development of central sensitization, and resulted in the recovery of mechanical hyperalgesia and allodynia.

Since local perfusion of the compressed DRG with lidocaine only partially prevented mechanical hyperalgesia, it suggests that there might be other factors, in addition to spontaneous activity, that contribute to the development of neuropathic pain behaviors. It has been well documented that, following peripheral nerve injury, abnormal adrenergic sensitivity has been developed in DRG neurons with intact or injured axons (Ali et al. 1999; Devor et al. 1994; Petersen et al. 1996; Sato and Perl 1991; Xie et al. 1995; Zhang et al. 1997). The sympathetic innervations of the DRG, which normally control the blood circulation, extend into the DRG to form basket-like structures around cell bodies (Chung et al. 1996; McLachlan et al. 1993; Ramer and Bisby 1997). Correspondingly, chemical or surgical sympathectomy can alleviate mechanical allodynia and other symptoms of neuropathic pain (Chung et al. 1996; Kim and Chung 1991; Lee et al. 1997). However, we cannot rule out the possibility that the perfusing rates for lidocaine as we emp...
ployed in the present study are sufficient to block all the abnormal activity originated in the compressed DRG.

It is not clear why the effects of lidocaine were greater on tactile allodynia than mechanical hyperalgesia. However, in an early study, LaMotte et al. (1991) found that tactile allodynia induced by intradermal injection of capsaicin could be abolished or significantly reduce by anesthetizing an area of skin centered on the capsaicin injection site. In contrast, the anesthetic was less effective in reducing mechanical hyperalgesia. These results have led LaMotte to hypothesize that the sensitization of central neurons receiving input from afferents activated by light stroking of the skin (allodynia) might be more dependent on a continual input of neural activity from the site of injury than the sensitization of neurons activated by punctate stimuli (hyperalgesia). Based on this hypothesis, it is expected that blocking the spontaneous activity originating in the compressed ganglion will greatly reduce allodynia, but may have lesser effect on the mechanical hyperalgesia.

If an upregulation of PN3/SNS TTX-resistant sodium channel also occurred in the compressed DRG as is observed in nerve-injured DRG neurons, then blockade of tactile allodynia by lidocaine may result from the suppression of TTX-resistant sodium channel in the injured Aβ-fiber neurons as reported by Scholz (1998).

In summary, the results of the present study demonstrate the feasibility of inducing mechanical hyperalgesia and allodynia by single-ganglion compression; further, mechanical hyperalgesia and allodynia can be reduced by local administration of lidocaine to the compressed ganglion. It is anticipated that this model will be useful in exploring and evaluating therapeutic approaches to patients suffering lumbar radiculopathy.

The authors thank Dr. Robert H. LaMotte, Yale University, for help in designing drug-perfusing systems.

This research study was supported by a Pilot Study Fund from the University of Arkansas for Medical Sciences.

The references are:

**REFERENCES**


**Bennett GJ. and Xie Y-K.** A peripheral mononeuropathy in rat that produces mechanical hyperalgesia and allodynia can be reduced by local administration of lidocaine to the compressed ganglion. It is anticipated that this model will be useful in exploring and evaluating therapeutic approaches to patients suffering lumbar radiculopathy.

**The authors thank Dr. Robert H. LaMotte, Yale University, for help in designing drug-perfusing systems.**

**This research study was supported by a Pilot Study Fund from the University of Arkansas for Medical Sciences.**

**REFERENCES**


**Scholz (1998).**


