

## SPINAL MANIPULATION REDUCES PAIN AND HYPERALGESIA AFTER LUMBAR INTERVERTEBRAL FORAMEN INFLAMMATION IN THE RAT

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### ABSTRACT

**Objective:** To document potential mediating effects of the Activator-assisted spinal manipulative therapy (ASMT) on pain and hyperalgesia after acute intervertebral foramen (IVF) inflammation.

**Methods:** The IVF inflammation was mimicked by in vivo delivery of inflammatory soup directly into the L5 IVF in adult male Sprague-Dawley rats. Thermal hyperalgesia and mechanical allodynia were determined by the shortened latency of foot withdrawal to radiant heat and von Frey filament stimulation to the hind paw, respectively. Intracellular recordings were obtained in vitro from L5 dorsal root ganglion (DRG) somata. DRG inflammation was examined by observation of the appearance and hematoxylin and eosin staining. ASMT was applied to the spinous process of L4, L5, and L6. A series of 10 adjustments were initiated 24 hours after surgery and subsequently applied daily for 7 consecutive days and every other day during the second week.

**Results:** (1) ASMT applied on L5, L6, or L5 and L6 spinous process significantly reduced the severity and duration of thermal and mechanical hyperalgesia produced by the IVF inflammation. However, ASMT applied on L4 did not affect the response in rats with IVF inflammation or the controls; (2) electrophysiological studies showed that hyperexcitability of the DRG neurons produced by IVF inflammation was significantly reduced by ASMT; (3) pathological studies showed that manifestations of the DRG inflammation, such as the increased vascularization and satellitosis, were significantly reduced 2 to 3 weeks after ASMT.

**Conclusions:** These studies show that ASMT can significantly reduce the severity and shorten the duration of pain and hyperalgesia caused by lumbar IVF inflammation. This effect may result from ASMT-induced faster elimination of the inflammation and recovery of excitability of the inflamed DRG neurons by improving blood and nutrition supplement to the DRG within the affected IVF. Manipulation of a specific spinal segment may play an important role in optimizing recovery from lesions involving IVF inflammation. (*J Manipulative Physiol Ther* 2006;29:5-13)

**Key Indexing Terms:** *Spinal Manipulation; Hyperalgesia; Inflammation*

Lumbar intervertebral foramen (IVF) inflammation appears to play a critical role in the pathogenesis of low back pain.<sup>1-3</sup> This process can produce injury or disease to the structures and tissues within and/or adjacent to the IVF.<sup>4-10</sup> After inflammation or nerve injury

or dorsal root ganglion (DRG) compression, the chemical factors such as cytokines, nerve growth factors, inflammatory mediators, and other substances release and activate and/or change the properties of DRG neurons and spinal dorsal horn neurons and contribute to hyperalgesia.<sup>4,5,7,11-15</sup> Nerve-injured or DRG-compressed sensory neurons, in vitro, exhibit enhanced responses to inflammatory mediators.<sup>4</sup> To further understand the mechanisms of low back pain due to IVF inflammation, we have recently developed an animal model of IVF inflammation produced by in vivo delivery of inflammatory mediators directly into the IVF at L5.<sup>16,17</sup> Rats with L5 IVF inflammation exhibit measurable pain and hyperalgesia and the primary sensory neurons become more excitable.

The mechanisms for the clinical effects of spinal manipulative therapy (SMT) are poorly understood but are

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thought to be related to mechanical, neurophysiological, and reflexogenic processes.<sup>18,19</sup> In addition to traditional manual SMT, instruments such as the Activator Adjusting Instrument (AAI) have also been used to produce spinal mobilization.<sup>20</sup> The AAI was developed to precisely control the speed, force, and direction of the adjustive thrusts so that one may produce a safe, reliable, and controlled force to adjust osseous spinal structures.<sup>21,22</sup> The AAI evolved in response to current knowledge in biomechanical and neurophysiological categories of investigation. Under the biomechanical model, issues such as tissue compliance (stiffness), response to input force (impedance), and natural frequency resonance of the spine were explored. In neurophysiological investigations, threshold frequencies and minimal forces required for stimulation of joint mechanoreceptors were investigated.<sup>20,23,24</sup>

The purpose of this study was to document potential mediating effects of SMT as performed using the AAI on pain and hyperalgesia produced by lumbar IVF inflammation in a small animal model with outcomes being assessed through behavioral, electrophysiological, and pathological approaches.

## METHODS

### Surgery

All experimental procedures were conducted in concordance with the recommendations of the International Association for the Study of Pain (IASP) and the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*. The procedures were reviewed and approved by the Institutional Animal Care Committee of Parker College Research Institute. Adult male Sprague-Dawley rats (200-250 g weight at start of the experiment,  $N = 148$ ) were used in this study. They were housed in groups of 4 to 5 in plastic cages measuring 40 × 60 × 30 cm with soft bedding and free access to food and water under a 12-hour day/12-hour night cycle. The rats were kept 3 to 5 days under these conditions before and up to 40 days for some animals after surgery. All surgeries were done under anesthesia induced by sodium pentobarbital (40 mg/kg IP, supplemented as necessary).

Intervertebral foramen inflammation was produced by in vivo delivery of inflammatory soup (IS) directly into the lumbar IVF at L5 in 100 rats. The procedure was the same as that previously described in our studies.<sup>16,17</sup> In brief, each rat was anesthetized and a midline incision was made from L4 to L6. On the left side, the paraspinal muscles were separated from the mammillary process and the transverse process and the L5 IVF exposed. A fine, sharp, stainless steel needle, 0.4 mm in diameter, attached with a microsyringe was inserted approximately 2 mm into the IVF at a rostral direction at an angle of approximately 30° to 40° to the dorsal midline and -10° to -15° to the vertebral horizontal line. The insertion was guided by the mammillary

process and the transverse process. As the needle was moved over the ganglion and/or the nerve, the ipsilateral hind leg muscles typically exhibited one or two slight twitches. Then the IS (30  $\mu$ L) containing bradykinin, 5-HT, histamine, and prostaglandin each in  $10^{-5}$  M at pH 7.35 or other vehicle was slowly injected (manually guided) into the IVF. After the needle was withdrawn, the muscle and skin layers were sutured. Of the 100 rats, 80 were used for behavioral testing and 12 and 8 received electrophysiological and morphological assessment, respectively.

In 48 rats, the surgical procedure was identical to that described for IVF inflammation but without needle stick. Of the total 48 rats, 40 were used for behavioral testing and 6 and 2 received electrophysiological and morphological assessment, respectively. An oral antibiotic, Augmentin, was administered in the drinking water for each rat (7.52 g in 500 mL) after surgery for 7 days.

### Behavioral Observations and Tests

The rats were tested on each of 2 successive days before surgery. After surgery, the animals were inspected every 1 or 2 days during the first 14 postoperative days and at weekly intervals thereafter. For general observation, the rats were placed on a table and notes were made on the animal's gait and the posture of each hind paw and the conditions of the hind paw skin.

The presence of thermal hyperalgesia was determined by measuring foot withdrawal latency to heat stimulation.<sup>14,15</sup> Each rat was placed in a box (22 × 12 × 12 cm) containing a smooth glass floor. The temperature of the glass floor was measured and maintained at 26°C + 0.5°C. A heat source (IITC Model 336 Analgesia Meter, Life Science, Series 8) was moved beneath a portion of the hind paw that was flush against the glass and a thermal stimulus was delivered to that site. The stimulus shut off automatically when the hind paw moved (or after 20 seconds to prevent tissue damage). The intensity of the heat stimulus was maintained constant throughout all experiments. The elicited paw movements were at a latency of approximately 9 to 12 seconds in control rats. Thermal stimuli were delivered 4 times to each hind paw at 5- to 6-minute intervals. Postoperative tests were made 1, 3, 4, 5, 7, 10, and 14 days after surgery and then once weekly for 5 weeks. For assessment of thermal hyperalgesia, the withdrawal latency on the contralateral side was subtracted from those on the experimental side and the result was expressed as a difference score.

The presence of mechanical allodynia was determined by measuring foot withdrawal threshold to mechanical indentation of the plantar surface of each hind paw with von Frey filaments.<sup>13</sup> The filaments capable of exerting forces of 10, 20, 40, 60, 80, and 120 mN, but each having the same tip diameter of 0.1 mm, were applied to 10 designated loci distributed over the plantar surface of the foot. During each test, the rat was placed in a transparent plastic cage with a floor of wire with openings measuring 1 × 1 cm. The cage

was elevated so that stimulation could be applied to each hind foot from beneath the rat. Each filament was applied alternately to each foot and to each locus. The filaments were applied in order of ascending force. The duration of each stimulus was 1 second and the interstimulus interval was approximately 10 to 20 seconds. The incidence of foot withdrawal was expressed as a percentage of the 10 applications of each stimulus as a function of force. The threshold was defined as the force corresponding to a 50% withdrawal, as determined by linear interpolation. To reduce preexisting differences among individuals in mechanical responsiveness, the withdrawal thresholds were also normalized by subtracting each value on the treated side from the corresponding value on the contralateral side and the results were expressed as difference scores. The testing schedule was the same as that in the thermal test.

### Electrophysiological Recording

Electrophysiological recordings were obtained in vitro from L5 DRG neurons from rats that received IVF inflammation ( $n = 6$ ), IVF inflammation plus Activator-assisted spinal manipulative therapy (ASMT) ( $n = 6$ ), and surgical control ( $n = 6$ ) during the period of 15 to 28 days after surgery. The rat was anesthetized with sodium pentobarbital. The sciatic nerve was isolated from surrounding tissue, transected at the mid-thigh level, and its proximal portion traced to the ganglia. A laminectomy was then performed and the L5 DRG and its dorsal roots were identified. Oxygenated artificial cerebrospinal fluid (ACSF), consisting of (in mmol/L) 130 NaCl, 3.5 KCl, 1.25  $\text{NaH}_2\text{PO}_4$ , 24  $\text{NaHCO}_3$ , 10 dextrose, 1.2  $\text{MgCl}_2$ , and  $\text{CaCl}_2$  ( $\text{pH} = 7.3$ ), was dripped periodically onto the surface of the ganglion during the surgical procedure to prevent drying and hypoxia. The ganglion was removed from the rat and placed in a 35-mm Petri dish filled with oxygenated ACSF. Under the dissecting microscope, the perineurium and epineurium were peeled away from the ganglion with fine forceps and the attached peripheral nerve and dorsal roots transected adjacent to the ganglion. The ganglion was then placed in the recording chamber and mounted on the stage of an upright microscope (BX50-WI, Olympus). A U-shaped stainless steel rod with 4 pieces of silver wire crossed from one side to the other was used to gently hold the ganglion in place within the recording chamber. The DRG was perfused continuously with oxygenated ACSF at a rate of 2 mL/min at room temperature.

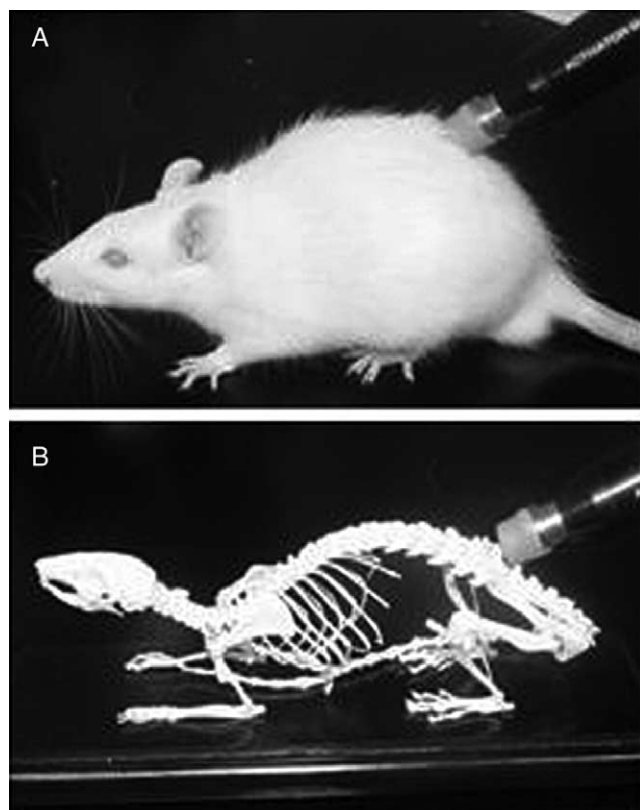
Intracellular, electrophysiological recordings were made from the L5 DRG somata using conventional bridge-balance techniques (Axoclamp-2B, Axon Instruments, Foster City, Calif) and analyzed with PCLAMP-8 under Windows 98 (Axon Instruments). Dorsal root ganglion cells were visualized under differential interference contrast in the microscope and the cell soma was classified visually by the diameter of its soma as small ( $\leq 30 \mu\text{m}$ ), medium

(31–49  $\mu\text{m}$ ), or large ( $\geq 50 \mu\text{m}$ ). The small cells are nociceptive cells and are somata of the unmyelinated C fibers that convey nociceptive information from peripheral terminals to the spinal cord or higher levels of central nervous system. The medium cells match A-delta fibers and mainly convey sharp and fast pain. The large cells match the big A-beta fibers and primarily convey nonnociceptive information, such as touch and light pressure. Glass microelectrodes were fabricated with a Flaming/Brown micropipette puller (Model P-97/PC, Sutter Instruments, Novato, Calif) and were filled with 2 M potassium acetate ( $\text{pH} = 7.2$ ). Satisfactory recordings were obtained with electrodes having DC resistances ranging from 20 to 60  $\text{M}\Omega$ .

For evaluating excitability of the DRG neurons, we examined resting membrane potential ( $V_m$ ), the action potential (AP) current threshold, and the repetitive discharge characteristics of the cells evoked by depolarizing current. The  $V_m$  was taken 2 to 3 minutes after a stable recording first obtained. Depolarizing currents of 0.05 to 2 nA (50 milliseconds duration) were delivered in increments of 0.05 nA (for small cells) or 0.1 to 0.2 nA (for medium and large cells) until an AP was evoked. Action potential current threshold was defined as the minimum current at 50 milliseconds duration required to evoke an AP. Repetitive discharge of each neuron was measured by counting the spikes evoked by intracellular injection of standardized depolarizing currents at  $2.5 \times$  threshold strength ( $\times 1000$  milliseconds). Discharge patterns of DRG neurons were classified into two types: (1) neurons firing either one or two APs and (2) neurons firing more than two APs.<sup>14,15</sup>

### Pathological Studies

The DRGs were taken from the rats at different periods of time (1–28 postoperative days). Appearance of the ganglia was observed under light microscope ( $\times 4$ ) and higher magnification ( $\times 40$ ) before electrophysiological recordings ( $n = 18$ ). From another 10 rats (2 control, 4 IVF inflammation, and 4 IVF inflammation with Activator treatment), the bilateral L5 DRGs were removed after the rats were anesthetized and perfused with 100 mL of heparinized saline followed by 400 mL 4% paraformaldehyde in phosphate buffer. The ganglia were post-fixed in the same fixative for 3 hours and then immersed in 30% sucrose overnight at  $4^\circ\text{C}$ . Frozen tissues were sectioned (15  $\mu\text{m}$  thick, Leica 1850) and stained with hematoxylin and eosin. We chose 4 (second, fourth, sixth, and eighth) of the total 10 sections from the layer of cells ( $\sim 200 \mu\text{m}$ ) in each ganglion to do further microscope analysis of the glia cells. Four grid areas were chosen from within each section. Each grid area (4  $\text{cm}^2$  under  $\times 10$  microscope) was used to count the glia cells, those located on the surface of the sections and could be identified under higher magnification ( $\times 40$ ). The counts obtained from these sampling boxes were determined and represent the number of cells per unit of the structure of

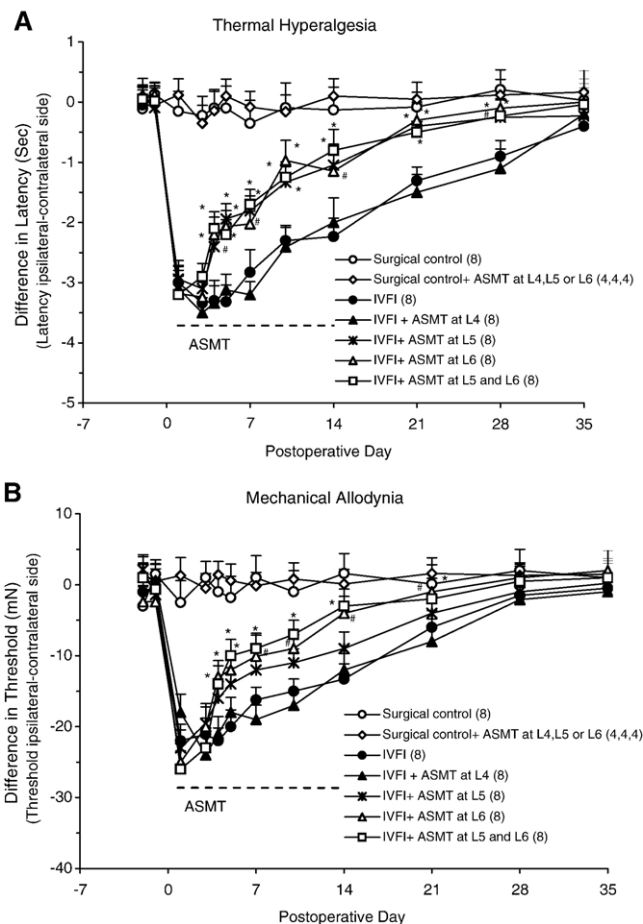


**Fig 1.** Method of the Activator-assisted spinal manipulative therapy applied to the lumbar spinous process in the rat. The location and direction of the Activator III applying on the lumbar spinous process are shown in a real experimental rat (A) and in an artificial rat skeleton (B).

interest. Finally, the data were calculated and converted into the numbers of glia cells in unit of  $1000 \mu\text{m}^2$  and expressed in the figure in the results.

#### Activator-Assisted Spinal Manipulative Therapy

The Activator III was used to model SMT. This adjustment delivers short-duration ( $<0.1$  milliseconds) mechanical force, manually assisted spinal manipulative thrusts. The adjustments were applied to the spinous process of L4, L5, L6, or both L5 and L6 in different groups of rats (see Results). Activator-assisted spinal manipulative therapy was applied at a rostral direction at an angle of approximately  $40^\circ$  to  $50^\circ$  to the vertebral horizontal line. A schematic of Activator adjustment is shown in Fig 1. A series of 10 adjustments was initiated 24 hours after surgery and subsequently applied daily for 7 consecutive days and every other day during the second week. Each adjustment included one single application of the Activator to the spinous process of the vertebra. For those that the adjustments were applied to both L5 and L6 spinous process, each adjustment included one single application of the AAI to the spinous process of L5 and L6, respectively.



**Fig 2.** Effects of the ASMT on thermal hyperalgesia and mechanical allodynia induced by IVF inflammation. A, Time course of thermal hyperalgesia (negative difference scores) after IVF inflammation and inhibition of hyperalgesia during and after treatment. B, Time course of mechanical allodynia (decreased mean threshold) after IVF inflammation and inhibition of hyperalgesia during and after AAI treatment. The numbers of animals tested in each group are shown in parentheses, with the numbers listed in order of ASMT at L4, L5, and L6 in the groups of "surgical control" in A and B. Data are expressed as mean  $\pm$  SEM. # $P < .05$ , \* $P < .01$ , 2-way repeated measurement of ANOVA followed by post hoc pairwise comparisons.

#### Statistical Analysis

Differences in mean mechanical threshold and the difference scores of the latency over time were tested with 2-way repeated measures analysis of variance (ANOVA) followed by post hoc paired comparisons. Between-animal group comparison of the score obtained on the given experimental day was with Mann-Whitney  $U$  test. One-way ANOVA followed by Dunnett tests were used to test the hypothesis that resting membrane potential and excitability of DRG neurons in IVF inflammation groups were significantly different from both the surgical control and Activator treatment groups. Individual  $t$  tests were used to

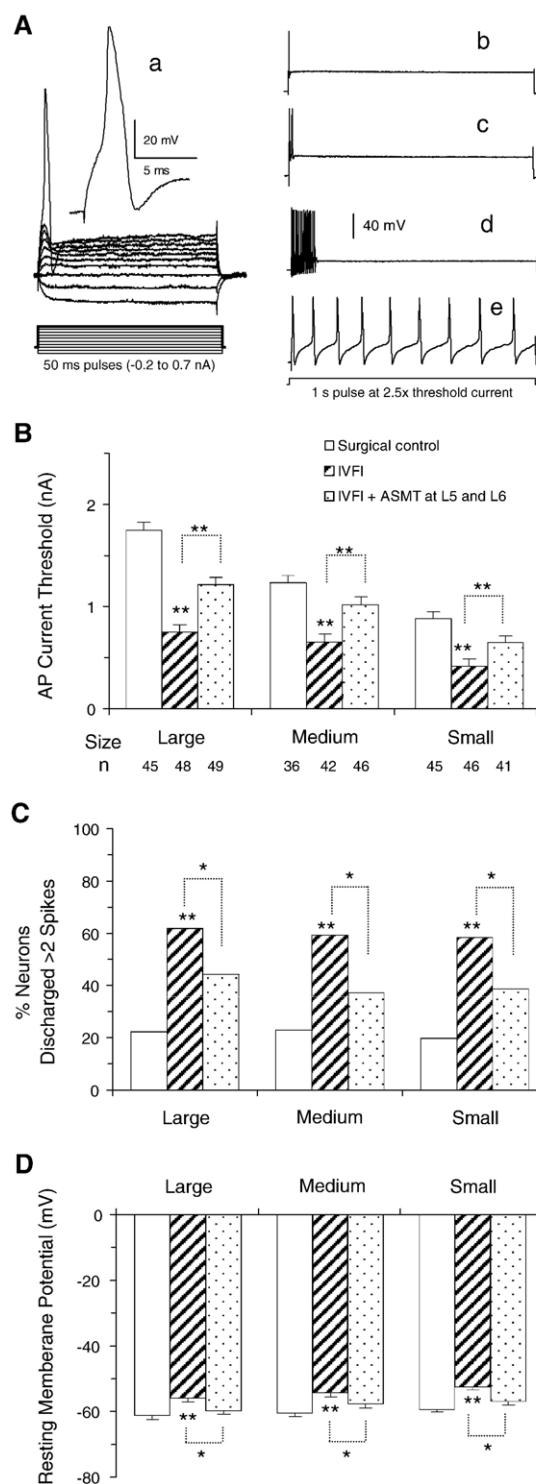


test specific hypothesis about differences between each IVF inflammation or with Activator treatment group and its corresponding surgical control group for each electrophysiological parameter tested.  $\chi^2$  Tests were used to identify differences in the incidence of effects. All data are presented as mean  $\pm$  SEM. Unless otherwise stated, statistical results described as significant are based on a criterion of a  $P$  value of less than .05.

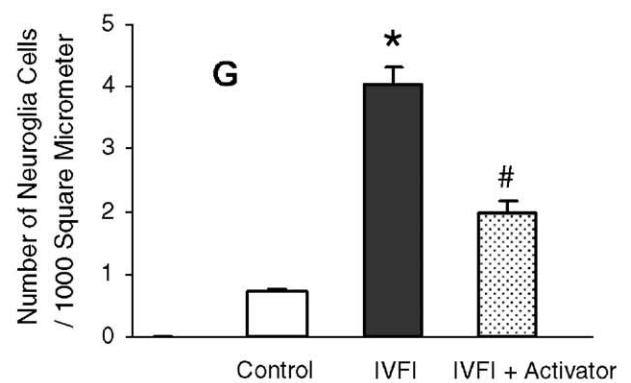
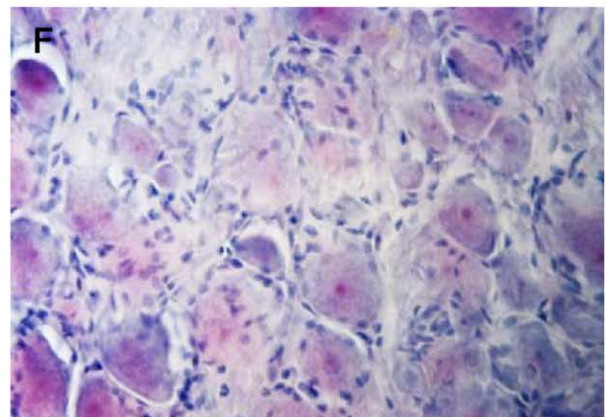
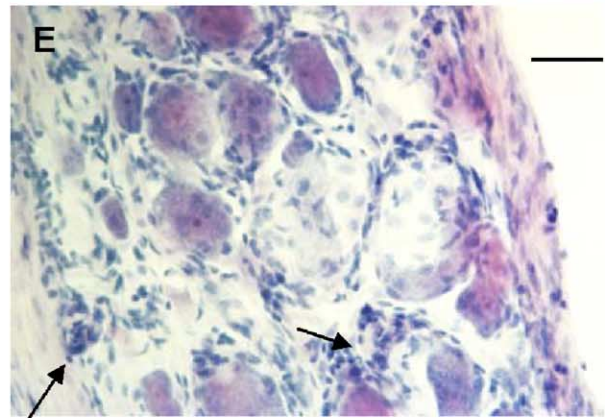
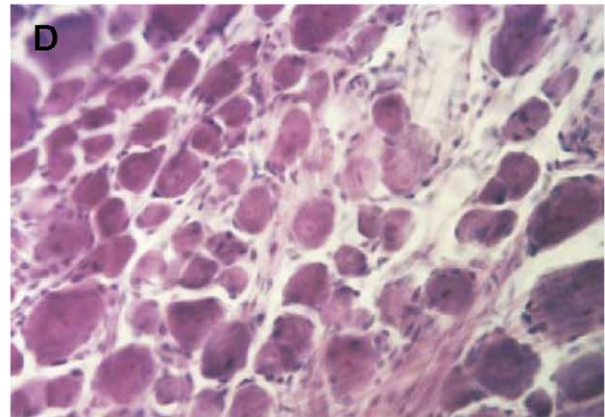
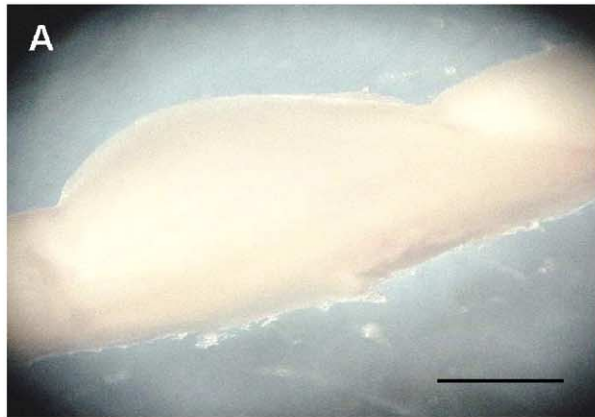
## RESULTS

### Effects of ASMT on IVF Inflammation-Induced Thermal Hyperalgesia and Mechanical Allodynia

The animals that received IVF injection of the IS exhibited significant thermal hyperalgesia and mechanical allodynia (the negative difference scores) as shown in Fig 2. The foot ipsilateral to the IVF inflammation became more sensitive to the thermal or mechanical stimulus, but the responses of the foot contralateral to IVF inflammation were not significantly changed (data not shown). ASMT applied on the spinous process significantly reduced the IVF inflammation-induced thermal hyperalgesia (Fig 2A) and mechanical allodynia (Fig 2B) in severity and duration. Severity of thermal hyperalgesia started to decrease significantly on the fourth post-injection day, that is, after 3 adjustments, evidenced by the increased latency of foot withdrawal to heat stimulation ( $\#P < .05$ ,  $*P < .01$ ). Duration of hyperalgesia was shortened to 2 to 3 weeks in the animals that received adjustments as compared with 4 to 5 in the control. ASMT applied on L5, L6, or both L5 and L6 showed similar effects. However, the adjustments on L4 neither improved the hyperalgesia in IVF inflammatory animals nor altered the normal response in controls (Fig 2A). ASMT applied on L5, L6, or both L5 and L6, but not L4, produced similar effects on the mechanical allodynia. The treatments reduced the severity and shortened duration of allodynia to 10 to 14 days from 3 to 4 weeks. ASMT applied on L5 produced less effect than that at L6 and both L5 and L6 and did not shorten the duration of mechanical allodynia (Fig 2B).



**Fig 3.** Effects of the ASMT on excitability and resting membrane potential of the inflamed DRG neurons. A, Examples of action potentials and cellular responses in DRG neurons evoked by the intracellular test protocol; a, Hyperpolarizing and depolarizing responses to 50 milliseconds current pulses (the largest depolarizing pulse reached threshold for evoking an action potential); b-e, discharge patterns in DRG neurons tested with 1-second pulses delivering 2.5x threshold current as described in the Methods. B-D, Activator adjustments reversed the decreased action potential current threshold (B) and increased incidence of repetitive discharge (C) and membrane depolarization in large, medium, and small DRG neurons after IVF inflammation.  $*P < .05$ ,  $**P < .01$  (B and D, Student  $t$  test; C,  $\chi^2$  test).



### Effects of ASMT on IVF Inflammation-Induced Hyperexcitability of the DRG Neurons

Electrophysiological studies showed that IVF inflammation of L5 caused hyperexcitability of the DRG neurons and such increased excitability was significantly reduced by ASMT. Fig 3 summarizes these effects and shows examples of electrophysiological responses to intracellular test stimuli applied to different sizes of DRG neurons (Fig 3A). After IVF inflammation, the mean AP current threshold decreased significantly in DRG neurons of all sizes ( $P < .01$ ,  $t$  tests, Fig 3B). Hyperexcitability of DRG neurons was also revealed as an enhancement of repetitive discharge evoked by a 50-millisecond depolarizing current pulse normalized to AP current threshold. Approximately 60% of the neurons from inflamed DRG responses with 3 or more APs to the normalized depolarizing current, and the rest exhibited 1 or 2 APs, whereas only around 20% of the neurons from control DRG discharged 3 or more APs ( $P < .01$  in each case,  $\chi^2$  tests, Fig 3C). In addition, the inflamed DRG neurons were significantly depolarized (Fig 3D). Two to 4 weeks after ASMT treatments, the increased excitability of the sensory neurons decreased and recovered significantly compared with those without treatment (Fig 3B-D).

### Effects of ASMT on the Pathological Changes of the Inflamed DRG

Under light dissecting microscope, the ganglion from the inflamed IVF showed clear signs of inflammation and it appeared to be covered by a layer of connective tissue that was somewhat difficult to remove, and increased vascularization could be seen on the surface of the ganglia. In contrast, the ganglion from control animals or contralateral to IVF inflammation looked clear and had no obvious blood vessels. Examples are given in Fig 4A-C. Hematoxylin and eosin staining again showed clear inflammatory signs in the DRG neurons from the rats with IVF inflammation. The DRG neurons were surrounded by significantly increased glia cells (data are summarized in Fig 4G). Satellitosis was observed in most of the slices (eg, Fig 4E). Satellitosis is a condition marked by an accumulation of glia cells around the neurons and is often as prelude of the neuronophagia (phagocytosis of nerve cells), which would finally result in cell death. Neuro-

nophagia and karyopyknosis (cytologic characteristics of the superficial or cornified cells of stratified squamous epithelium in which there is shrinkage of the nuclei and condensation of the chromatin into structureless masses) were sometimes observed in the inflamed, but not the control ganglia (data not shown). Three to 4 weeks after ASMT, such expression of DRG inflammation was significantly reduced (Fig 4F-G) compared with those without (Fig 4E). We did not find obvious inflammation in the ganglia contralateral to the inflammation.

### DISCUSSION

The present study investigated the effects of instrumented assisted SMT on pain and hyperalgesia produced by acute IVF inflammation in L5 in a small animal model by means of behavioral, electrophysiological, and pathological approaches. We found that the AAI-assisted SMT applied to the IVF inflamed spinous process can significantly reduce the severity and shorten the duration of pain and hyperalgesia, reduce the hyperexcitability of the DRG neurons, and alleviate inflammation of the DRG neurons after the IVF inflammation.

Inflammatory responses play key roles in behavioral hyperalgesia and hyperexcitability of DRG cells in inflammatory pain as well as in neuropathic pain.<sup>7-11</sup> Intervertebral foramen inflammation is one of the main reasons for low back pain. After IVF inflammation, the chemical factors such as cytokines, nerve growth factors, inflammatory mediators, and other substances release and activate and/or change the properties of DRG neurons and spinal dorsal horn neurons as well as increase their excitability and therefore contribute to pain and/or hyperalgesia.<sup>4,5,7</sup> In the present study, injection of the inflammatory mediators into the IVF directly produces acute inflammation to the constituents within the IVF, that is, DRG, nerve root, and blood and lymph vessels, and, furthermore, may produce ischemia and compromise the delivery of oxygen and nutrients. Interestingly, our studies show that ASMT can significantly alleviate the symptoms and shorten the duration of pain and hyperalgesia caused by the IVF inflammation. Furthermore, by means of electrophysiological and pathological assessments, our

**Fig 4.** Changes in appearance of the DRG and the neurons within after IVF inflammation (IVFI) and the ASMT. A-C, Images of the appearance of the ganglia 3 weeks after IVF inflammation with or without treatment under light dissecting microscope. A, The L5 ganglion contralateral to the inflamed IVF (control). B, The inflamed L5 ganglion with increased vascularization on the surface. C, The inflamed L5 ganglion after Activator treatment. D-F, Hematoxylin and eosin-stained DRG neurons 3 weeks after IVF inflammation with or without treatment ( $\times 40$ ). D, L5 ganglion contralateral to the inflamed IVF. The DRG neurons (big cells sized from approximately 10 to 60  $\mu\text{m}$ ) and the glia cells are shown. E, L5 ganglion from the inflamed IVF. The glia cells increased significantly (G). A large amount of glia cells surrounded the DRG neurons and formed the phenomenon of "satellitosis" (arrows). F, L5 ganglia from the inflamed IVF after Activator treatment. The increased glia cells were significantly reduced. G, Summary of effects of Activator treatment on the inflammation of DRG neurons characterized with the changes in the amount of neuroglia cells. \* $P < .01$  ( $t$  test, compared between groups of control IVFI and IVFI [IVFI + Activator]), # $P < .01$  ( $t$  test, compared between groups of control [IVFI + Activator] and IVFI [IVFI + Activator]). Scales: 1 mm (left) and 40  $\mu\text{m}$  (right).



studies showed that the faster relief of pain and hyperalgesia after ASMT may result from the faster recovery of hyperexcitability of the sensory neurons and elimination of the DRG inflammation.

Although the mechanism of action of this intervention is unknown, there are numerous possibilities. It was found that the lumbar vertebrae experienced an axial displacement, posteroanterior shear displacement, and rotational displacement at the upper spinal segment levels. Coupled spinal motion was also detected in more than just the vertebra receiving a direct thrust.<sup>20</sup> In our present study, the AAI was applied to the small animal with IVF inflammation and produced significant treatment effects on the pain and hyperalgesia. Based on the findings of research on Activator adjustments on a human spine, the increased movement of the affected intervertebral joints (facets) and the coupled spinal motion may contribute to the treatment effect of Activator via improving the blood and nutrition supply to the DRG within the affected IVF.

In addition, chiropractic adjustments delivered by the AAI may "normalize" articular afferent input to the central nervous system with subsequent recovery of muscle tone, joint mobility, and sympathetic activity.<sup>25,26</sup> It was also hypothesized that a chiropractic lumbar thrust would produce sufficient force to coactivate all of the mechanically sensitive receptor types,<sup>27</sup> and adjustments made with the AAI are thought to accomplish the same task.<sup>28</sup> An Activator adjustment may have the capacity to coactivate type III, high-threshold mechanoreceptors. Both types III and IV receptors in diarthrodial joints, as well as type II in paravertebral muscles and tendons, are responsive to vertebral displacement.<sup>29</sup> In addition, Activator adjustment may be effective by activating the receptors in the spinal cord and some of the ascending and descending signaling pathways that involve pain modulation.<sup>30</sup> These may contribute to the mechanisms underlying the treatment effects of the AAI.

The importance of specificity as it relates to which spinal segment or segments are manipulated has been a long-standing debate within the chiropractic profession. Most treatment techniques emphasize the importance of manipulation of a specific vertebral segment.<sup>31</sup> The general belief is that specific adjustments are therapeutically superior to general mobilization. Recent studies suggest several problems with specific chiropractic adjustments. First, chiropractors appear to be unable to accurately palpate and identify the spinal segment they often seek to target.<sup>32</sup> Secondly, due to the size of the contact points on the physician's hand, there is a question regarding the ability to deliver specific force to the specific area of the spine where it is intended. The present studies are important in addressing the issue of treatment specificity. However, through literature reviews, we could not locate evidence to support or refute that primary question of whether making contact on specific vertebrae is in fact important. This

research is believed to be the first demonstration that reduced hyperalgesia from DRG inflammation was significant in animals where manipulation included the specific lumbar vertebrae and not in animals that were treated only at an adjacent vertebral segment. This study suggests that specificity was an important treatment variable in reducing hyperalgesia in this DRG inflammation model.

## CONCLUSION

The present study shows that ASMT can significantly reduce the severity and shorten the duration of pain and hyperalgesia caused by lumbar IVF inflammation. This effect may result from the adjustment-induced faster elimination of the inflammation and recovery of excitability of the inflamed DRG neurons. The ASMT may produce more movement of the affected intervertebral joints (facets), which may improve blood and nutrition supply to the DRG within the affected IVF. Our study also suggests that treating a specific vertebral level may be an important variable in chiropractic practice.

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