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Review Article

Neurophysiological effects of spinal manipulation

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Abstract

Background context: Despite clinical evidence for the benefits of spinal maniputation and the apparent wide usage of it, the biological mechanisms underlying the effects of spinal manipulation are not known. Although this does not negate the clinical effects of spinal manipulation, it hinders acceptance by the wider scientific and health-care communities and hinders rational strategies for improving the delivery of spinal manipulation.

Purpose: The purpose of this review article is to examine the neurophysiological basis for the effects of spinal manipulation.

Study design: A review article discussing primarily basic science literature and clinically oriented basic science studies.

Methods: This review article draws primarily from the peer-reviewed literature available on Medline. Several textbook publications and reports are referenced. A theoretical model is presented describing the relationships between spinal manipulation, segmental biomechanics, the nervous system and end-organ physiology. Experimental data for these relationships are presented.

Results: Biomechanical changes caused by spinal manipulation are thought to have physiological consequences by means of their effects on the inflow of sensory information to the central nervous system. Muscle spindle afferents and Golgi tendon organ afferents are stimulated by spinal manipulation. Smaller-diameter sensory nerve fibers are likely activated, although this has not been demonstrated directly. Mechanical and chemical changes in the intervertebral foramen caused by a herniated intervertebral disc can affect the dorsal roots and dorsal root ganglia, but it is not known if spinal manipulation directly affects these changes. Individuals with herniated lumbar discs have shown clinical improvement in response to spinal manipulation. The phenomenon of central facilitation is known to increase the receptive field of central neurons, enabling either subthreshold or innocuous stimuli access to central pain pathways. Numerous studies show that spinal manipulation increases pain tolerance or its threshold. One mechanism underlying the effects of spinal manipulation may, therefore, be the manipulation's ability to alter central sensory processing by removing subthreshold mechanical or chemical stimuli from paraspinal tissues. Spinal manipulation is also thought to affect reflex neural outputs to both muscle and visceral organs. Substantial evidence demonstrates that spinal manipulation evokes paraspinal muscle reflexes and alters motoneuron excitability. The effects of spinal manipulation on these somatosomatic reflexes may be quite complex, producing excitatory and inhibitory effects. Whereas substantial information also shows that sensory input, especially noxious input, from paraspinal tissues can reflexively elicit sympathetic nerve activity, knowledge about spinal manipulation's effects on these reflexes and on end-organ function is more limited.

Conclusions: A theoretical framework exists from which hypotheses about the neurophysiological effects of spinal manipulation can be developed. An experimental body of evidence exists indicating that spinal manipulation impacts primary afferent neurons from paraspinal tissues, the motor control system and pain processing. Experimental work in this area is warranted and should be encouraged to help better understand mechanisms underlying the therapeutic scope of spinal manipulation. © 2002 Elsevier Science Inc. All rights reserved.

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Introduction

Recent reports estimate that 7.7% to 8.3% of the US population uses some form of complementary or alternative medicine [1–3]. Approximately 30% to 40% of these individuals likely receive spinal manipulation [1]. Strong evidence supports using spinal manipulation to help patients with acute low back pain and neck pain [4,5]. The benefits of spinal manipulation for other disorders, such as chronic low back pain and visceral disorders, are less clear, although benefits have been noted [4,6–8]. Despite the clinical evidence for the benefits of and the apparent wide usage of spinal manipulation, the biological mechanisms underlying the effects of spinal manipulation are not known. Although this does not negate the clinical effects of spinal manipulation, it hinders acceptance by the wider scientific and health-care communities and hinders rational strategies for improving the delivery of spinal manipulation. The purpose of this review article is to examine the neurophysiological basis for and the neurophysiological effects of spinal manipulation.

Biomechanical considerations of spinal manipulation

Spinal manipulation by its very nature is a mechanical input to tissues of the vertebral column. Chiropractors deliver more than 90% of these manipulations in the United States [9]. Spinal manipulation is distinguished from spinal mobilization in several ways [10]. During spinal manipulation, the practitioner delivers a dynamic thrust (impulse) to a specific vertebra. The clinician controls the velocity, magnitude and direction of the impulse [11]. The art or skill of spinal manipulation lies in the clinician's ability to control these three factors once the specific contact with a vertebra is made. Mobilization techniques are sometimes used preparatory to the manipulation. Manipulation is also distinguished from mobilization in that it is delivered at or near the end of the physiological range of motion (the so-called paraphysiological range [12]) but not exceeding the anatomical limits of motion. A cracking or popping sound often, but not necessarily, accompanies the manipulation, because gapping the joint creates fluid cavitation [13,14].

The most common form of spinal manipulation used by chiropractors is the short-lever, high-velocity and low-amplitude thrust [15]. The clinician usually delivers the dynamic thrust through a short-lever arm by manually contacting paraspinal tissues overlying the spinous, transverse or mammillary processes of the vertebra being manipulated. Alternatively, the clinician contacts tissues overlying the lamina or articular pillar of the vertebra. To manipulate the pelvis, the iliac spine or the ischial spine is used [10]. Spinal manipulation may also be delivered through a long-lever arm. While one hand may contact a specific area over the vertebra being manipulated, the second hand contacts an area of the body distant from the specific contact. Force is developed through this long-lever arm. However, using a short-lever arm applied directly over the vertebra minimizes the force necessary to accomplish the manipulation [10] by reducing the amount of compliant tissue through which the force must be transmitted.

Several laboratories have studied biomechanical features of short-lever, high-velocity and low-amplitude manipulation. Herzog's group [16] was the first to report the biomechanical features of a spinal manipulation in an indexed journal. They identified two characteristics common to the delivery of a spinal manipulation: 1) a preload force followed by 2) a larger impulse force. Using two chiropractors, they quantified the preload and peak impulse forces applied perpendicular to the contact point and the impulse duration during manipulation of the sacroiliac joint. Preload load forces ranged from 20 to 180 N, and peak forces ranged from 220 to 550 N. Often the preload was approximately 25% of impulse load. The duration of the high-velocity impulse ranged from 200 to 420 ms.

A number of studies have confirmed the force–time profile initially described by Hessel et al. [16]. Herzog et al. [17] showed the time to peak impulse was similar during manipulation of the thoracic spine and sacroiliac joint (approximately 150 ms$\pm$77 ms, mean$\pm$ SD). The perpendicularly applied preload and peak impulse forces were also similar during spinal manipulations applied to the thoracic (139$\pm$46 N vs. 88$\pm$78 N, respectively) and sacroiliac (328$\pm$78 N vs. 399$\pm$119 N, respectively) regions. Studies of the cervical spine indicate that preload, peak impulse force and time to peak impulse are less compared with the thoracic and lumbosacral spine [17–19]. Depending upon the type of cervical manipulative technique used, preload forces range from 0 to approximately 50 N, and peak impulse forces range from approximately 40 N to approximately 120 N. The forces delivered during cervical manipulations develop faster than during manipulation of the thoracic spine and sacroiliac joint. Impulse duration lasts from approximately 30 ms to approximately 120 ms. The large variability in the applied forces and durations should be recognized. The impact of this variability on the biological mechanisms that could contribute to the clinical effects of manipulation is unknown.

A complete understanding of the biomechanics of spinal manipulation requires knowing the manner in which manipulative loads are transmitted to a specific vertebra. Experimentally, this is substantially more difficult and more complex compared with measuring applied loads. Transmitted loads may be different from applied loads because of the effects of patient positioning and the contributions from inertial loads, loading moments and the active and passive properties of the intervening connective and muscle tissues. Triano and Schultz [20] calculated peak transmitted loads at a lumbar segment by measuring loads transmitted to a force plate placed under the subject. The force plate was capable of transducing forces and moments about three orthogonal axes. Peak forces transmitted to a lumbar segment during a side posture spinal manipulation tended to be higher than peak forces applied during a prone thoracic or sacroiliac manipulation measured by Herzog et al. [17]. Transmitted

impulse durations were similar to applied impulse durations measured by Herzog et al. [17]. Peak transmitted moments were approximately three to four times less than peak transmitted forces. The transmitted loads were considered below a threshold level capable of injuring the lumbar spine (see [20] for further discussion).

In addition to applied and transmitted loads, the relative displacement or movement between contiguous vertebrae during a spinal manipulation has been studied. Nathan and Keller [21] measured intervertebral lumbar motion using pins inserted into lumbar spinous processes. Manipulations were delivered using a mechanical adjusting device (Activator Adjusting Instrument, Activator Methods International, Ltd., Phoenix, AZ [22]). Impulse duration using this device is approximately 5 ms, an impulse duration shorter than that from manual manipulation. Impulses delivered to the L2 spinous produced 1.62 mm±1.06 mm peak axial displacement (in the longitudinal plane), 0.48±0.1 mm shear displacement (in the transverse plane) and 0.89±0.49° of rotation between L3 and L4 [21]. Smith et al. [23] measured similar vertebral displacements in the lumbar spine of the dog. L2 translated 0.71±0.03 mm and rotated 0.53±0.15° on L3 with impulse loads of 53 N. Gal et al. [24] performed measurements in the thoracic spine, but their results are difficult to compare with those reported above for the lumbar spine. Nonetheless, the movements induced during a spinal manipulative load suggest that mechanical processes may play a role in the biological effects of spinal manipulation.

Neurophysiological and biomechanical mechanisms underlying the effects of spinal manipulation

Numerous theories have been proposed to explain the effects of spinal manipulation [25,26]. A thread common to many of these theories is that changes in the normal anatomical, physiological or biomechanical dynamics of contiguous vertebrae can adversely affect function of the nervous system. [27,28]. Spinal manipulation is thought to correct these changes.

Accordingly, a number of biomechanical changes produced by vertebral movement during a spinal manipulation have been hypothesized. The mechanical force introduced into the vertebral column during a spinal manipulation may directly alter segmental biomechanics by releasing trapped meniscoids, releasing adhesions or by reducing distortion of the annulus fibrosus [29–33]. In addition, individual motion segments can buckle, thereby producing relatively large vertebral motions that achieve a new position of stable equilibrium [34]. The mechanical changes elicited by manipulation may provide sufficient energy to restore a buckled segment to a lower energy level, thus reducing mechanical stress or strain on soft and hard paraspinal tissues [35]. A major consequence of these hypothesized mechanical changes elicited by manipulation could be the restoration of zygapophyseal joint mobility and joint play [31]. In fact, authoritative discussion of spinal manipulation considers “the goal of manipulation to restore maximal, pain-free movement of the musculoskeletal system” (from [35a] and see [31,36,37]).

Biomechanical changes caused by the manipulation are thought to have physiological consequences by means of their effects on the inflow of sensory information to the central nervous system [25,36]. By releasing trapped meniscoids, discal material or segmental adhesions, or by normalizing a buckled segment, the mechanical input may ultimately reduce nociceptive input from receptive nerve endings in innervated paraspinal tissues. This would be consistent with the observation that spinal manipulation is not painful when administered correctly. In addition, the mechanical thrust could either stimulate or silence nonnociceptive, mechanosensitive receptive nerve endings in paraspinal tissues, including skin, muscle, tendons, ligaments, facet joints and intervertebral disc [28,38,39]. These neural inputs may influence pain-producing mechanisms as well as other physiological systems controlled or influenced by the nervous system.

Fig. 1 diagrams the theoretical relationships between spinal manipulation, segmental biomechanics, the nervous system and end-organ physiology. A biomechanical alteration between vertebral segments hypothetically produces a biomechanical overload the effects of which may alter the signaling properties of mechanically or chemically sensitive neurons in paraspinal tissues. These changes in sensory input are thought to modify neural integration either by directly affecting reflex activity and/or by affecting central neural integration within motor, nociceptive and possibly autonomic neuronal pools. Either of these changes in sensory input may elicit changes in efferent somatomotor and visceromotor activity. Pain, discomfort, altered muscle function or altered visceromotor activities comprise the signs or symptoms that might cause patients to seek spinal manipulation. Spinal manipulation, then, theoretically alters the inflow of sensory signals from paraspinal tissues in a manner that improves physiological function. This explanation comprises one of the most rational neurophysiological bases for the mechanisms underlying the effects of spinal manipulation. Experimental efforts to understand sensory processing from paraspinal tissues and the effects of spinal manipulation on this sensory processing is receiving increasing attention, as described below. Each of the following sections addresses a component of the theoretical relationship depicted in Fig. 1 with each section’s number corresponding to a numbered component in the figure.

1. The effects of spinal manipulation on sensory receptors in paraspinal tissues

Group I and II afferents (proprioceptive afferents)

Korr [36] proposed that spinal manipulation increases joint mobility by producing a barrage of impulses in muscle spindle afferents and smaller-diameter afferents ultimately silencing facilitated γ motoneurons. Fig. 2 shows the neural circuitry of the γ loop. He hypothesized that γ-motoneuron discharge is elevated in muscles of vertebral segments responding to spinal manipulation. The high gain of the γ

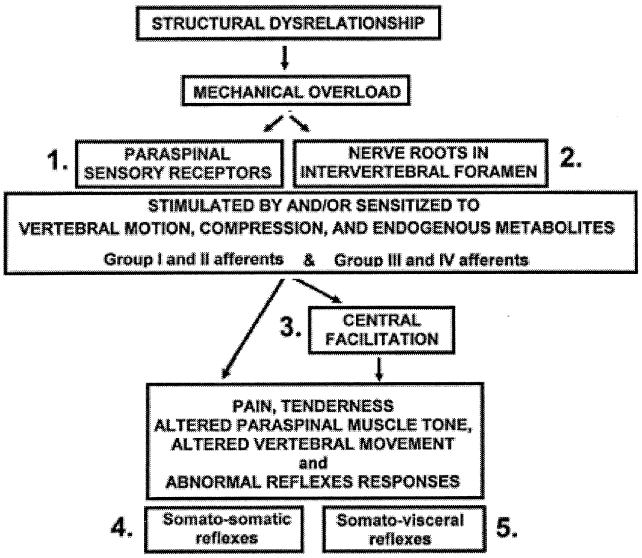

Fig. 1. A theoretical model showing components that describe the relationships between spinal manipulation, segmental biomechanics, the nervous system and physiology. The neurophysiological effects of spinal manipulation could be mediated at any of the numbered boxes.

loop would impair joint mobility by sensitizing the stretch reflex to abnormally small changes in muscle length. Korr further hypothesized that spinal manipulation stimulates muscle spindle afferents, that is, Group Ia and possibly Group II afferents (Table 1). The barrage of impulses from these afferents produced by the spinal manipulation would reduce the gain of the γ loop through an undetermined neural pathway. Although portions of this mechanism remain speculative, the contribution of proprioceptive afferents to spine function and the neurophysiological effects of spinal manipulation on these afferents are receiving increasing attention.

The importance of paraspinal proprioceptive input to the function of the vertebral column, and of the lumbar spine in particular, has been demonstrated recently in humans. Several studies indicate that muscle spindle input from the lumbar multifidus helps to accurately position the pelvis and lumbosacral spine. Healthy individuals can accurately reposition their lumbosacral spine, but their repositioning ability is impaired when the multifidus muscle is vibrated [40]. Vibration stimulates muscle spindles and creates a sensory illusion that the multifidus is stretched and therefore that the spine is flexed more than it actually is. The repositioning error occurs because of the misperception of vertebral position. Interestingly, lumbosacral-repositioning ability is impaired in individuals with a history of low back pain, even in the absence of vibration [41]. This finding was associated with altered proprioceptive input from muscle spindles [41]. In addition, paraspinal muscles in individuals with a history of low back pain also have longer response times to sudden loads, which also suggests the presence of abnormal paraspinal proprioceptive input in these individuals [42–44].

Two experimental models have been developed recently that should enhance our neurophysiological understanding of the lumbar and cervical spine in general and of spinal manipulation specifically [45,46]. The experimental preparations enable the recording of neural activity from paraspinal tissues under conditions where controlled mechanical loads can be applied to an individual vertebra. The discharge properties of primary afferents with receptive fields in paraspinal tissues and the effects of these sensory inputs on neurons in the spinal cord can be determined. The preparations isolate the spinous process of a cervical [45] or lumbar [46] vertebra and use a servo-driven motor to control the displacement of or force applied to the spinous process. These preparations will enable neurophysiological studies not possible in humans.

Recent findings using one of the experimental models described above [46] demonstrate that spinal manipulation modifies the discharge of Group I and II afferents. Pickar and Wheeler [47] recorded single-unit activity from muscle spindle and Golgi tendon organ afferents having receptive fields in the lumbar multifidus and longissimus muscles

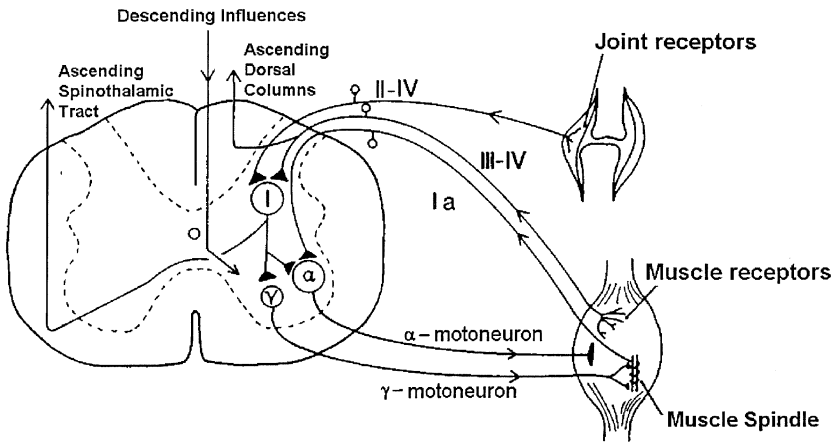

Fig. 2. Schematic showing the sensory pathways that could modulate γ motoneuron discharge. High-frequency discharge from muscle spindles input may affect descending input to the γ motoneurons. In addition, input from the smaller-diameter Group III and IV neurons may affect γ motoneurons.

Table 1
Classification of receptive nerve endings and their parent nerve fibers

Type of receptive ending	Location	Innervation	Conduction velocity (m/s)
Proprioceptors (specifically, muscle	Muscle	Group Ia, Ib (Aα) afferents	80–120
spindles and Golgi tendon organs)	Muscle	Group II (Aβ) afferents	35–65
Low-threshold mechanoreceptors	Muscles, joints, skin	Group II (Aβ) afferents	35–65
	Muscles, joints, ligaments, skin	Group III (Aδ) afferents	2.6–30
	Muscles, joints, ligaments, skin	Possibly Group IV (C) afferents	⩽2.5
High-threshold mechanoreceptors	Muscles, joints, skin	Group II afferents	35–65
	Muscles, joints, ligaments, skin	Group III (Aδ) afferents	2.6–30
	Muscles, joints, ligaments, skin	Group IV (C) afferents	⩽2.5
Chemoreceptors and thermoreceptors	Muscles, joints, skin	Group III (Aδ) afferents	2.6–30
	Muscles, joints, ligaments, skin	Group IV (C) afferents	⩽2.5

while applying a spinal manipulative-like load to a lumbar vertebra. Golgi tendon organ afferents were generally silent at rest and were activated more by the impulsive thrust of a spinal manipulation than by the static load preparatory to the thrust. Their silence resumed at the end of the manipulation. Muscle spindles generally had a resting discharge that also increased more to the impulse than to the preload (200% compared with 30%). The spindles were silenced for 1.3 seconds on average after the manipulative impulse. In addition, a presumed Pacinian corpuscle responded to the impulse of a manipulative-like load but not to loads with a slower force–time profile. The discharge of these three types of afferents may represent a portion of the neural discharge recorded by Colloca et al. [48] during spinal manipulation in an anesthetized human patient undergoing an L4–L5 laminectomy. They recorded multiunit activity from the intact S1 nerve root during spinal manipulations of the lumbosacral region using a low-force, short-duration (impulse) loading apparatus (ie, Activator Adjusting Instrument [22]).

Group III and IV afferents

Electrophysiological recordings from Group III and IV afferents innervating the spine of rats, rabbits and cats have helped us understand the mechanical and chemical stimuli that can excite the receptive endings of sensory paraspinal neurons. Cavanaugh et al. [49] recorded afferent activity from the medial branch of the dorsal primary rami after removing the superficial and deep lower back muscles in the rat. Gentle probing of the facet capsule elicited a slowly adapting discharge, whereas forceful pulling on the supraspinous ligament elicited a slowly adapting discharge from afferents in the lumbar spine. The forces applied to these tissues were not quantified. The afferents from which Cavanaugh et al. [49] recorded were likely slowly conducting, that is, Group III and/or Group IV afferents, but classification based on single-unit conduction velocities was not obtained. Pickar and McLain [50] recorded single-unit activity from Group III (conduction velocity, 9.0±6.6 m/s) and Group IV (conduction velocity, 1.5±0.5 m/s) afferents with receptive fields in feline lumbar paraspinal tissues. They measured the response of these small-diameter neurons to movement of the L5–L6 facet joint. The majority of afferents, including seven with receptive fields in or near the facet joint capsule, responded in a graded fashion to the direction of a nonnoxious load applied to the joint. Yamashita et al. [51] found that only 20% of Group III afferents in and around the lumbar facet joint had high mechanical thresholds (greater than 8.5 gm), as determined with von Frey–like hairs. This latter finding contrasts with afferents studied in the cervical spine, where almost all Group III afferents studied had high mechanical thresholds [52]. However, Yamashita et al. [51] further showed that substance P increases the resting discharge and decreases the von Frey threshold by +80% and −30%, respectively, of the afferents in and around the lumbar facet joint. This suggests that inflammation may decrease the mechanical thresholds of receptive endings around a lumbar facet joint. Again, this contrasts with the discharge properties of Group III afferents in the cervical region, which were not sensitive to the inflammatory mediator bradykinin [52]. To date, there have been no studies investigating the effects of spinal manipulation on the discharge properties of small-diameter, thinly myelinated and unmyelinated sensory neurons innervating paraspinal tissues.

The studies cited above make it reasonable to think that spinal manipulation may add a novel sensory input or remove a source of aberrant input. Gillette [28] presented a speculative yet comprehensive analysis of the receptive nerve endings potentially affected by spinal manipulation. He suggested that 40 types of mechanoreceptive endings in the skin and deep tissues of the paraspinal region could be activated, because they have mechanical thresholds below the level of mechanical force applied during a manipulation. The mechanoreceptors include proprioceptors (muscle spindles, both primary and secondary endings and Golgi tendon organs), low-threshold mechanoreceptors, high-threshold mechanoreceptors, high-threshold mechanonociceptors and high-threshold polymodal nociceptors [28]. Thus, all classifications of sensory neurons, that is, Group Ia, Ib, II, III and IV fibers (Table 1), could be affected, theoretically, by spinal manipulation.

2. The effects of spinal manipulation on neural tissue within the intervertebral foramen

The spinal roots within the intervertebral foramen (IVF) possess unusual anatomical properties, having less connective tissue support and protection compared with peripheral nerve [53,54]. As the peripheral nerve trunk enters the IVF, its epineurium separates from the trunk and becomes continuous with the dura mater. Perineurium surrounding individual fascicles is lost as the fascicles separate into ventral and dorsal roots. Endoneurium surrounding the individual Schwann cells that ensheath both the myelinated and unmyelinated axons continue into the nerve roots, but the endoneurium's collagen content becomes less dense and is no longer organized as a protective sheath [55]. In addition, the density of Na^+ channels in the soma and initial segment of dorsal root ganglia cells is relatively high, suggesting these regions may be unusually excitable [56]. These properties may render neural tissue within the IVF vulnerable to effects of mechanical compression and the chemical environment produced by changes in the intervertebral disc or facet joints [57].

Substantial evidence demonstrates that the dorsal roots (DRs) and dorsal root ganglia (DRG) are more susceptible to the effects of mechanical compression than are the axons of peripheral nerves, because impaired or altered function is produced at substantially lower pressures [57,58]. Compressive loads as low as 10 mg applied rapidly to the DRs slightly increases the discharge of Group I, II, III and IV afferents [58]. Slowly repeated loads or gradually increasing loads produce conduction block [58,59]. Maintained compressive pressures as low as 20 mm Hg applied to the DRs cause conduction block [60]. Although the DRs are not as sensitive as the DRGs to mechanical pressure, prior mechanical injury greatly increases resting DR discharge. In contrast, only slight mechanical compression applied to the DRG is sufficient to produce large, prolonged increases in the discharge of Group I, II, III and IV afferents even in the absence of prior mechanical injury [58,59,61].

Mechanical compression of the DRs or DRG, in addition to altering impulse-based neural transmission (ie, action potentials), may alter non–impulse-based mechanisms (eg, axoplasmic transport). This biological concept was introduced into the literature of spinal manipulation nearly a quarter century ago [60]. Applying as little as 10 mm Hg pressure to the DRs reduces by 20% to 30% nutritional transport to the peripheral axons as measured by tracer-labeled glucose [62]. DR compression reduces the transport rate of the neuropeptide substance P but not vasointestinal peptide [63]. In addition, DRG compression increases endoneurial fluid pressure and is accompanied by edema and hemorrhage within the DRG [64].

Compression studies, like those described above, laid experimental groundwork for investigating how herniated intervertebral discs affect nerve root function. Clearly, the idea that a herniated disc could directly compress the DRs or DRG is straightforward. Recently, pressure between a herniated disc and the nerve root was measured in 34 humans undergoing surgery for lumbar disc herniation [65]. Mean pressures of 53 mm Hg (range, 7 to 256 mm Hg) were measured. A second idea describing how herniated intervertebral discs could affect nerve root function suggests that its effects are mediated indirectly by the release of neuroactive chemicals [66]. This mechanism would help explain the common observation that, even in the absence of compression, herniated discs are accompanied by neurological findings. Recent studies demonstrate that the application of nucleus pulposus to a lumbar nerve root causes mechanical hyperalgesia in the distal limb and causes swelling in and decreased blood flow to the DRG [67,68]. In addition, phospholipase A_2 (PLA_2), an inflammatory mediator associated with disc herniation [66,69], is neurotoxic in high doses to Group I, II, III and IV [61]. In moderate doses it increases mechanical sensitivity of the DRs, producing long-lasting discharge, and it increases the discharge of previously silent DRG cells [61,70].

Whereas increasing evidence demonstrates that the mechanical and chemical consequences of a herniated disc can affect neural tissue within the IVF, no studies were found investigating the effects of spinal manipulation on the mechanical or chemical environment of the IVF. Whether spinal manipulation can alter neural function by mechanically changing compressional pressures or reducing the concentration of metabolites in the IVF is unknown. However, several case studies [35,71,72] and randomized clinical studies [73,74] show that spinal manipulation of patients with herniated intervertebral discs can be followed by clinical improvements. These findings warrant further investigation. Without adequate basic science studies, it will be difficult to determine the mechanism of action underlying observed clinical improvements.

3. The effects of spinal manipulation on central facilitation

Central facilitation (also called central sensitization) refers to the increased excitability or enhanced responsiveness of dorsal horn neurons to an afferent input. Central facilitation can be manifested by increased spontaneous central neural activity, by enhanced discharge of central neurons to an afferent input or by a change in the receptive field properties of central neurons [75].

Denslow et al. [76] were one of the first groups of investigators to systematically study the neural organization of tender areas in paraspinal tissues. Their findings lead to one of the predominant rationales for the clinical use of spinal manipulation, namely, the premise that persistent alterations in normal sensory input from a functional spinal unit increases the excitability of neuronal cells or circuits in the spinal cord [25,36,76]. They observed that muscles with firm texture, which accompany postural abnormalities, show electromyographic (EMG) characteristics different from muscles with normal texture. Either spontaneous EMG activity was present or EMG activity could be induced unlike the normal area [77,78]. In subsequent studies, Denslow et al. [76,79] showed that reflex erector spinae activity evoked by pressure placed

against paraspinal tissues varied between subjects and between vertebral segments. The patterns they observed suggested that α motoneurons could be held in a facilitated state because of sensory bombardment from segmentally related paraspinal structures. The motor reflex thresholds also correlated with pain thresholds, further suggesting that some sensory pathways were also sensitized or facilitated in the abnormal segment [76].

We currently know that the phenomenon of central facilitation increases the receptive field of central neurons and allows innocuous mechanical stimuli access to central pain pathways [80]. In other words, subthreshold mechanical stimuli may initiate pain, because central neurons have become sensitized. Removal of these subthreshold stimuli should be clinically beneficial. One mechanism underlying the clinical effects of spinal manipulation may be the removal of subthreshold stimuli induced by changes in joint movement or joint play (see previous section: Neurophysiological and biomechanical mechanisms underlying the effects of spinal manipulation). In addition, nonnoxious mechanical inputs themselves can also have therapeutic effect. The gate control theory of Melzack and Wall [81] drew attention to the active role of the dorsal horn of the spinal cord. The dorsal horn is not simply a passive relay station for sensory messages but can modulate the messages as well. Numerous studies inspired by Melzack and Wall's theory clearly demonstrate that nonnoxious mechanical inputs travelling by means of the large, myelinated A fiber neurons can inhibit the response of dorsal horn neurons to nociceptive stimuli from C fibers (reviewed in [82]). Natural activation of A-α and A-β fibers (Table 1) has been shown to reduce chronic pain and increase pain threshold levels (reviewed in [82]). If such a gate mechanism contributes to the effects of spinal manipulation, the means by which such a short-lasting nonnoxious mechanical input produces a long-lasting effect needs to be understood.

Effects on pain and pain processing

Numerous studies suggest that spinal manipulation alters central processing of innocuous, mechanical stimuli, because pain tolerance or threshold levels increase. In patients with low back pain, Glover et al. [83] examined areas of lumbar skin that were painful to a pinprick. Fifteen minutes after spinal manipulation of the lumbar region, the size of the area from which the pinpricks evoked pain was reduced compared with the control group receiving detuned short-wave therapy. Terrett and Vernon [84] quantified the reduction in pain sensitivity after spinal manipulation. They established a model of pain sensation using graded, electrical stimulation of cutaneous paraspinal tissues. A blinded observer assessed the minimal current necessary to evoke pain (pain threshold) and the maximal tolerable current that evoked pain (pain tolerance) in subjects with tender regions of the thoracic spine. Spinal manipulation significantly increased (1.5-fold) pain tolerance levels within 30 seconds. Over the next 9.5 minutes, tolerance levels progressively increased (up to 2.4-fold; Fig. 3).

Continued efforts to determine and quantify the effects of spinal manipulation on nociceptive processing have made use of the pressure algometer. The reliability and validity of this pressure gauge have been demonstrated [85,86]. Vernon [87] measured changes in the pressure/pain threshold after spinal manipulation using this device sensation. The pressure/pain threshold represents the magnitude of the pressure at which the subject reports that the sensation of pain changes to a sensation of tenderness. In this case study, spinal manipulation increased the average pressure/pain threshold of six tender spots in the neck region by approximately 50% (from 2 kg/cm^2 to 2.9 kg/cm^2). In a study of the lumbar spine, neither spinal manipulation nor spinal mobilization changed the pressure/pain thresholds at three standardized locations in patients with chronic mechanical low back pain [88]. The standardized locations were myofascial trigger points associated with low back pain but were not necessarily clinically relevant (ie, tender) to the patient. These latter results, when compared with those from Vernon's study [87], could suggest that physiological responses to spinal manipulation are specific to regions of the vertebral column. Alternatively, the results suggest that the neurophysiological effects of spinal manipulation on pain processing will be understood only when symptomatic sites are chosen based on their degree of tenderness or painfulness to the patient. Overall, the findings are provocative and warrant continued investigation. If spinal manipulation initiates changes in the central facilitatory state of the spinal cord, then understanding the relationship between biomechanical inputs to and the neurophysiological responses from paraspinal tissues will enable us to optimize the delivery of these manipulations.

The effect of spinal manipulation on pain could also be mediated by the neuroendocrine system. The endogenous opiate

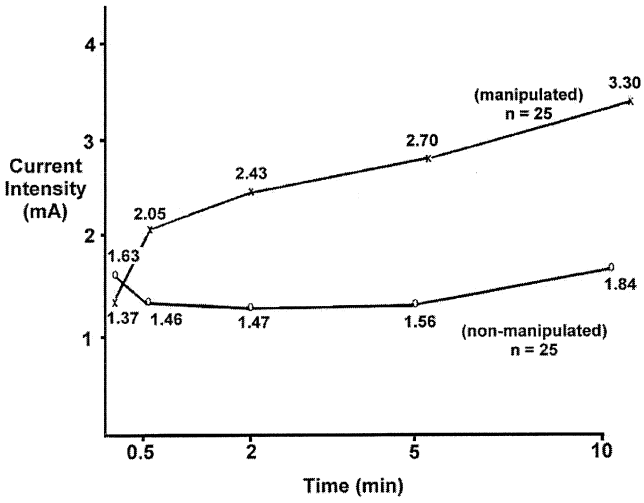

Fig. 3. Increased pain tolerance threshold after spinal manipulation. Threshold determined by the electrical current necessary to evoke maximal endurable pain. (From [84], Reprinted with permission).

system is known to modify pain processes [89], and a number of therapeutic modalities, including acupuncture [90], transcutaneous nerve stimulation [91] and exercise [92], are thought to exert pain-relieving effects through activation of this system. Several studies have investigated the effect on spinal manipulation on circulating levels of β-endorphin. The findings have been inconsistent for possible reasons discussed by Rosner [93]. Vernon et al. [94] reported an 8% increase in plasma β-endorphin levels 5 minutes after spinal manipulation but not after control interventions. Christian et al. [95] did not find any change in plasma β-endorphin levels, but their assay would have been unable to detect an 8% increase because their between-assay variation was greater than the 8%. On the other hand, Sanders et al. [96] did not find any change in plasma β-endorphin levels despite a reduction in the visual analog pain scale in the group receiving spinal manipulation. Anti–pain-producing effects of β-endorphin can be mediated by their ability to bind to membrane-bound receptors on sensory nerve endings in the periphery as well as to receptors in the spinal cord and brain. However, the relationship between circulating levels of β-endorphin and the release of β-endorphin in the spinal cord is not known [97]. Thus, while the experiments cited may indicate a response mediated by peripheral receptors, the effects of spinal manipulation on β-endorphin release within the central nervous system are unknown.

4. The effects of spinal manipulation on somatosomatic (muscle) reflexes

Substantial evidence demonstrates that spinal manipulation evokes paraspinal muscle reflexes and alters motoneuron excitability. In asymptomatic patients. Herzog's group [98,99] showed that posterior to anterior spinal manipulative treatments applied to the cervical, thoracic lumbar and sacroiliac regions increased paraspinal EMG activity in a pattern related to the region of the spine that was manipulated. The EMG response latencies occur within 50 to 200 ms after initiation of the manipulative thrust. Similarly, spinal manipulation using an Activator Adjusting Instrument applied to a transverse process elicits paraspinal EMG activity at the same segmental level but within 2 to 3 ms [22]. Colloca and Keller [100] confirmed these latter findings in symptomatic patients with low back pain. In addition, they reported that the increased EMG activity, while beginning within 2 to 3 ms of the manipulation, reached its peak within 50 to 100 ms. EMG activity representing a strong reflex response in terms of peak amplitude was relatively long lived (greater than 273 ms), whereas EMG activity representing weak reflex responses was more short lived (less than 273 ms). Paraspinal EMG responses were greatest in magnitude when the manipulation was delivered close to the electrode site and, interestingly, the more chronic the low back pain, the less the EMG response. It is important to note that the EMG electrodes were not placed relative to any physical finding associated with the low back, for example, a presumed site of muscle spasm or a site of muscle pain or tenderness.

The effect of spinal manipulation on paraspinal muscle activity is not only excitatory. In one symptomatic patient with spontaneous muscle activity in the thoracic spine, Suter et al. [99] observed reduced paraspinal EMG activity within 1 second after a thoracic spinal manipulation. DeVocht obtained similar findings in a symptomatic patient with low back pain (Fig. 4, unpublished observations). He placed EMG electrodes over palpably taut lumbar paraspinal muscles and often observed a decrease in spontaneous EMG activity after spinal manipulation using an Activator Adjusting Instrument and treatment protocol. The decreased muscle activity did not occur instantaneously.

The effects of spinal manipulation on somatomotor activity may be quite complex, producing excitatory and inhibitory effects. It is worth noting that many of the individual human studies cited above were performed on either symptomatic or asymptomatic individuals but not both. In addition, EMG recordings were sometimes obtained from standardized sites and in other studies were obtained relative to clinical findings of taut muscle fibers. Paradoxical findings may be reconciled if future studies compare the effects of spinal manipulation on symptomatic versus asymptomatic subjects and on anatomical sites with clinically identified or quantified signs. Clearly, the potential for spinal manipulation to inhibit motor activity can

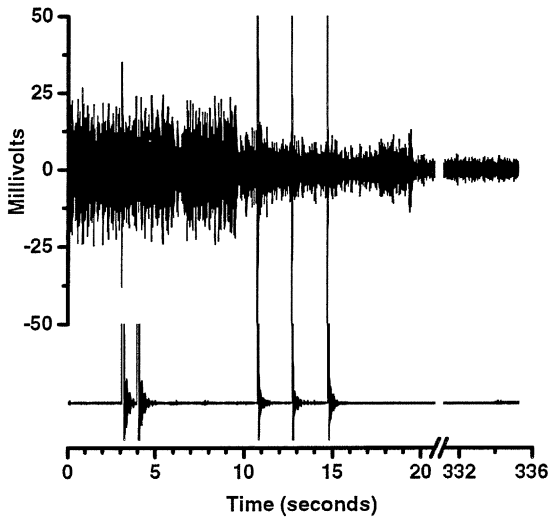

Fig. 4. Original data from a subject showing spontaneous paraspinal muscle activity in the lower lumbar spine and its response to spinal manipulation. Electromyographic (EMG) activity (top trace) decreased in response to spinal manipulation using an Activator Adjusting Instrument and treatment protocol. A tripolar, disposable, adhesive EMG electrode was placed approximately 2 to 3 cm to the right of the L4 spinous process over paraspinal muscle that was taut when palpated. Bottom trace is the output from an accelerometer attached to the head of the Activator Adjusting Instrument. Large accelerometer spikes represent the onset of each spinal manipulative impulse. Spinal manipulation was applied three times to the sacral base (third manipulation not obtained from the accelerometer) and successively applied to the L5, L4 and L3 mammillary processes. The large spikes in the top trace are likely mechanical artifacts from the manipulative impulse. (Unpublished observations.)

be determined only under experimental conditions where muscle activity is spontaneously present or has been evoked.

The effects of spinal manipulation on paraspinal EMG activity may be associated with increases in muscle strength measured after spinal manipulation. Suter et al. [101] studied symptomatic patients with sacroiliac joint dysfunction, anterior knee pain and evidence of motor inhibition to knee extensor muscles. A side posture spinal manipulation applied to the sacroiliac joint significantly decreased the inhibition of the knee extensors on the side of the body to which the manipulation was applied. Similarly, Keller and Colloca found that erector spinae isometric strength (assessed using EMG activity) was increased after spinal manipulation compared with sham manipulation [102]. In neurophysiological terms, these two studies indicate that spinal manipulation improves muscle function either through facilitation or disinhibition of neural pathways.

A series of studies has sought to understand how spinal manipulation affects central processing of motor control information. The studies indicate that spinal manipulation can both increase the excitability of motor pathways in the spinal cord and depress the inflow of sensory information from muscle spindles. In asymptomatic patients, Dishman et al. [103] showed that spinal manipulation increases central motor excitability (Fig. 5). EMG activity from gastrocnemius muscle evoked by direct activation of descending corticospinal tracts using transcranial magnetic stimulation was larger after lumbar spinal manipulation compared with simply positioning the patient but not applying the manipulation. Spinal manipulation also depresses the H reflex. Manipulation applied to the sacroiliac joint in a posterior to anterior direction decreased the magnitude of the tibial nerve H reflex for up to 15 minutes in asymptomatic humans [104]. Similarly, side-posture lumbar manipulation of L5–S1 joint inhibited the H reflex from the tibial nerve [105]. The effects of mobilization alone applied to the same joint were similar, but the effects of manipulation tended to be greater. After manipulation alone, the inhibition lasted for approximately 20 seconds but lasted up to 1 minute when manipulation was preceded by spinal mobilization. These contrasting effects on EMG activity, between methodologies using motor evoked potentials versus the H reflex, may reflect the differential effects of sensory input evoked by spinal manipulation on postsynaptic processing versus presynaptic inhibition, respectively (see, for extensive discussion, Dishman et al. [103].

One possible mechanism contributing to spinal manipulation's inhibitory effects on the H reflex and on spontaneous paraspinal EMG activity is suggested by recent experiments. Sensory input from facet joint tissues stimulated during spinal manipulation might reflexively decrease paraspinal muscle activity. Indahl et al. [106] elicited reflex longissimus and multifidus muscle (EMG) activity by electrically stimulating the intervertebral disc in a porcine preparation. Stretching the facet joint by injecting 1 ml physiological saline abolished the EMG activity.

There is reason to believe that stretching the facet joint capsule and surrounding tissues likely occurs during spinal

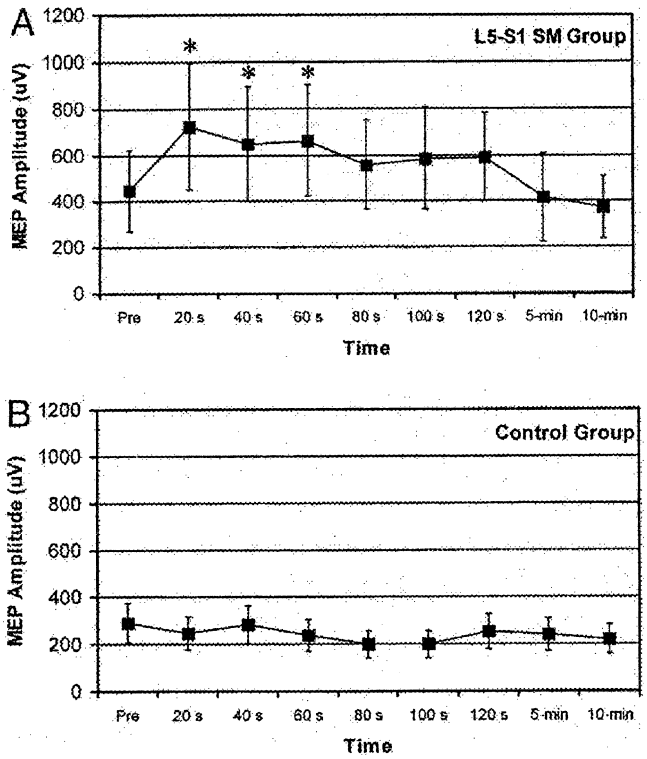

Fig. 5. Effects of spinal manipulation on motor evoked potentials in the gastrocnemius muscle. Muscle activity was evoked using transcranial magnetic stimulation applied near the vertex of the skull. Side posture spinal manipulation was applied on the right to L5–S1. During control, individuals were positioned in side posture but not manipulated. MEP=motor evoked potential; Pre=before manipulation or positioning; SM=spinal manipulation. (Reprinted with permission from J Manipulative Physiol Ther [103]).

manipulation, although this has received little study [107]. Using magnetic resonance imaging scans in human subjects, Cramer et al. [108] demonstrated that a side-posture spinal manipulation, accompanied by cavitation, gaps the facet joints. The synovial space of the lumbar facet joints increased in width by up to 0.7 mm in individuals receiving manipulation compared with nonmanipulated controls. The length of time between manipulation and the magnetic resonance imaging scan was not reported. In a study of the metacarpophalangeal joint, 5 minutes after cavitation joint separation was still increased by 0.4 mm and did not return to precavitation dimensions until 10 minutes after "cracking" [109]. It remains to be shown if joint separations of these magnitudes are sufficient to load the facet joint tissues. If so, this raises the possibility that tissues surrounding the facet joint could be stretched for periods of time longer than the duration of the manipulation itself. Graded sensory input from tissues surrounding the facet joint [50] could elicit reflex muscle responses similar to that measured by Indahl et al. [106].

Changes in muscle spindle input produced by spinal manipulation could also contribute to the inhibition of somatosomatic reflexes. Using magnetic stimulation, Zhu et al. [110,111] stimulated lumbar paraspinal muscles and recorded the evoked cerebral potentials. Stimulation of paraspinal mus-

cle spindles using vibration reduced the magnitude of the cerebral potentials. Similarly, muscle spasm in human patients reduced the magnitude of the paraspinal muscle–evoked cerebral potentials. Spinal manipulation reversed these effects, improving muscle spasm and restoring the magnitude of the evoked cerebral potentials [111], suggesting that increased sensory input from paraspinal muscle spindles during muscle spasm may contribute to the reduced magnitude of the evoked cerebral potentials. It is worthwhile recalling Korr's ideas [36] that spinal manipulation increases joint mobility by producing a barrage of impulses in muscle spindle afferents and smaller-diameter afferents, ultimately silencing facilitated γ motoneurons (see previous section: The effects of spinal manipulation on sensory neurons innervating paraspinal tissues; Group I and II afferents [proprioceptive afferents]).

At first it seems counterintuitive that muscle spindle discharge is increased during muscle spasm, because one could anticipate muscle shortening and spindle unloading during spasm. However, extensive studies from Proske's laboratory (reviewed in [112]) show that a maintained joint position or maintained muscle shortening, even for short durations, alters muscle spindle sensitivity to subsequent joint movement or muscle stretch. For example, from a given muscle length, muscle spindles respond more to a slow stretch when a leg muscle has previously been held at a shortened length compared with having been previously held at a long length for as little as 10 seconds [113]. Recently, Pickar and Kang [114] observed the same phenomenon in the lumbar longissimus and multifidus muscles (Fig. 6). Muscle spindle activity in response to a slow vertebral translation that stretched the muscle spindle depended on whether the muscle had previously been shortened for as little as 5 seconds (by linearly displacing the L6 vertebra dorsalward) or had previously been stretched (by linearly displacing the L6 vertebra ventralward). If paraspinal muscle spasm results in muscle shortening, or if segmental buckling results in muscle shortening ipsilaterally and muscle lengthening contralaterally, then for the same change in muscle length subsequent stretch or vibration of the affected muscles would increase spindle discharge more than expected. Because spinal manipulation has been shown to stimulate muscle spindles (Fig. 7), spinal manipulation may normalize spindle biomechanics and return muscle spindle discharge to normal.

5. The effects of spinal manipulation on somatovisceral reflexes

A number of animal experiments provide evidence supporting the link between altered paraspinal sensory input and a somatovisceral change shown in Fig. 1. Sensory input from paraspinal tissues can evoke visceral reflexes affecting the sympathetic nervous system and may alter end-organ function. In general, nonnoxious paraspinal sensory input appears to have an inhibitory effect on sympathetic outflow, whereas noxious input appears to have an excitatory effect. However, insufficient experiments have been conducted to determine the regional variation of this effect, that is, the change in sympathetic outflow to different organs. Nonetheless, the data are provocative, indicating that neural input from axial tissues can evoke somatovisceral reflexes.

Sato and Swenson [115] applied a nonnoxious mechanical stimulus to several vertebrae in the thoracic and lumbar

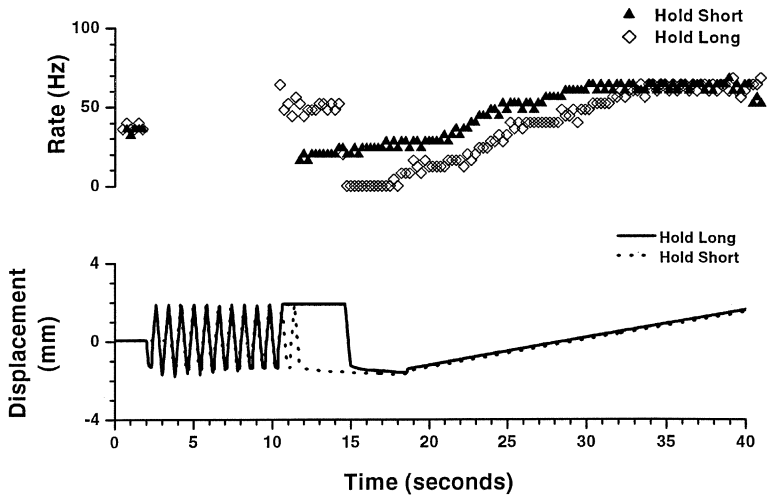

Fig. 6. Paraspinal muscle spindle sensitivity to identical changes in vertebral displacement is determined by the previous short-term history of its muscle's length. The receptive field of the muscle spindle was in the lumbar multifidus muscle. Top panel shows the discharge frequency of the muscle spindle afferent recorded from the L6 dorsal root. Instantaneous discharge frequency was averaged into 25-ms bins. The bottom panel shows the amount the L6 vertebra was displaced during flexion (negative displacement) and extension (positive displacement). These displacements shortened and stretched the multifidus muscle, respectively, because holding the L6 vertebra in an extended position (12 to 15 seconds) increased spindle discharge frequency compared with control. Conversely, holding the L6 vertebra in a flexed position (11 to 15 seconds) decreased spindle discharge frequency compared with control. Spindle discharge was the same at the start of the protocols (control, 0 to 2 seconds). The rapid extensions and flexions at the start of each protocol provided the same initial conditions. (Spindle discharge is not shown during these displacements). Top panel shows the change in muscle spindle sensitivity to the slow vertebral extension (18.5 to 40 seconds) after holding the multifidus muscle in shortened ▲ and stretched ◇ positions. Note that vertebral position was held for as little as 5 seconds. (Reprinted with permission from J Neuromusculoskel Sys, Data Trace Publishing Company [114]).

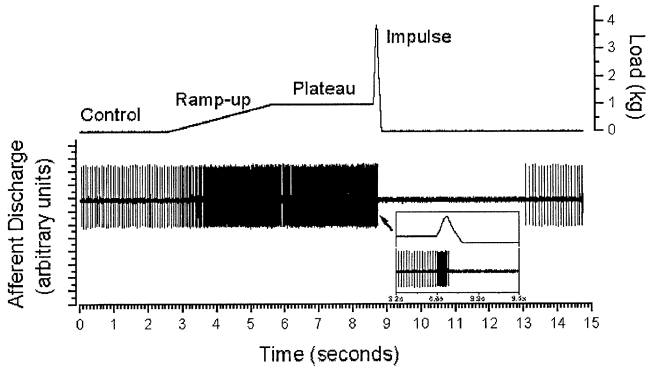

Fig. 7. Original tracing of a muscle spindle's response to a spinal manipulative-like load. The single unit activity was obtained from a muscle spindle afferent in the L6 dorsal root. The muscle spindle was located in the lumbar paraspinal muscles. Inset shows the spindle's discharge on an expanded time scale immediately before, during and shortly after the impulse. (From [47] Reprinted with permission.)

spine of rats by applying a force to the lateral aspects of their spinous processes. Renal and adrenal sympathetic nerve activities were recorded. Because the paraspinal musculature was removed, the sensory input was derived presumably from the facet joints, intervertebral discs and/or intervertebral ligaments. The mechanical stimulus reflexively decreased the level of renal and adrenal sympathetic nerve activity by 25% to 40%. The stimuli were short in duration (approximately 30 seconds), and the responses attenuated rapidly. The sensory input from the paraspinal tissues had access to centers at least as high as the upper cervical spinal cord, because C1–C2 spinal cord transection abolished the inhibition. Sato and Swenson concluded that nonnoxious mechanical stimuli applied to the spine reflexively inhibit the level of sympathetic nerve activity by means of a supraspinal reflex.

Budgell et al. [116,117] also stimulated paraspinal structures using noxious and nonnoxious chemical stimuli. Injections were placed into the lumbar facet joints or lumbar interspinous tissues. Blood pressure and sciatic nerve blood flow were measured [116]. A small volume (20 ul) of a nonnoxious chemical (physiological saline 0.9%) injected into the interspinous ligament produced a depressor response and a concomitant decrease in sciatic nerve blood flow. A similar volume of low-dose capsaicin (2 ug), which activates nociceptive neurons [118], caused an initial increase in blood pressure and sciatic nerve blood flow. However, when injected into the facet joint, capsaicin produced a depressor response. The results from the interspinous ligament are consistent with the suggestion offered by Sato and Swenson [115] that stimulation of receptive endings sensitive to innocuous mechanical stimuli in the paraspinal tissues produce inhibitory somaticsympathetic reflexes. The findings from the facet joints suggested to the authors that capsaicin might more effectively produce innocuous mechanical changes in the facet joint compared with the interspinous ligament by increasing the permeability of the synovial membrane's microvasculature. Similar to the cardiovascular effects produced by capsaicin injection into the lumbar interspinous ligament, capsaicin injection into the lumbar interspinous tissues also increased adrenal sympathetic nerve activity and catecholamine secretion [117], whereas physiological saline injection had no effect. Thus, noxious stimulation of paraspinal tissues can produce excitatory somatic-sympathetic reflexes.

More recently, Pickar et al. [119], in a preliminary report, showed that mustard oil, a nociceptive substance that also produces inflammation, injected into the lumbar multifidus muscle increases the discharge of sympathetic nerves to the kidney and spleen. The response is a reflex mediated by segmental branches of the dorsal ramus and is integrated by centers at least as high as the upper cervical spinal cord. This reflex organization is similar to that found by Sato and Swenson [115] for the sympathetic nerves to the kidney and adrenal gland. Interestingly, animal studies have also shown that increased splenic sympathetic nerve discharge is immunosuppressive, decreasing the number of natural killer cells released. Somatovisceral reflex stimulation of the sympathetic outflow to the spleen may contribute to the depressed levels of natural killer cells measured in individuals with low back pain [120].

Mechanical stimulation of paraspinal tissues can be sufficient to inhibit gastric motility. Myoelectric activity from the wall of the gastrointestinal tract in conscious rabbits was decreased by sustained (2.5 minutes) mechanical inputs [121]. In these experiments, it was unclear if the mechanical stimulation was noxious or innocuous, but the inhibition of gastric motility was greatest when the mechanical stimulation was applied to the sixth thoracic vertebra, and it decreased as the mechanical stimulation was applied further cranial or caudal. These results were confirmed by Budgell and Suzuki [122]. Noxious chemical stimulation inhibited gastric motility, and the effect tended to be greater when the stimulus was applied to the mid-thoracic region compared with the lumbar region. In addition, the inhibitory response was shown to be a reflex predominated by changes in sympathetic outflow and to a lesser extent vagal outflow.

It is important to note that these studies do not provide evidence for the unique potential of paraspinal tissues to elicit somatosympathetic reflexes. Substantial evidence shows that noxious stimulation of tissues in the appendicular skeleton also evokes somatosympathetic reflexes [123], but nothing is known about the relative magnitudes of somatosympathetic reflexes elicited by axial versus appendicular tissues. Although the data on gastric motility suggest segmental specificity, it is not certain the degree to which segmental input from paraspinal tissues produce regionally specific changes in sympathetic nerve activity.

Very few laboratory or clinically oriented basic science studies have been conducted to determine the effects of spinal manipulation on the sympathetic nervous system. Recently, Budgell and Hirano [124] measured changes in heart rate variability after upper cervical versus sham spinal manipulation. Power spectral analysis of heart rate variability showed that manipulation increased the ratio of low fre-

Table 2
Current evidence for the neurophysiological mechanisms underlying the effects of spinal manipulation

Mechanism	Current evidence		
	In favor	Negative	Unknown
Alters Group Ia and Group II mechanoreceptor discharge	X		
Alters Group III and Group IV mechanoreceptor or chemoreceptor discharge			X
Alters mechanical environment of the IVF			X
Alters chemical environment of the IVF			X
Influences sensory processing in the spinal cord (ie, central facilitation)	X		
Affects neuroendocrine system	X	X	
Impacts control of skeletal muscle reflexes (ie, somatosomatic reflexes)	X		
Impacts control of autonomic reflexes (ie, somatovisceral reflexes)			X

IVF = intervertebral foramen.

quency to high frequency components indicating a possible shift in the balance of autonomic control of the heart toward the parasympathetic nervous system.

Spinal manipulation may alter the response of immunologic cells as well as the production of immunomodulatory and neuromodulatory cytokines. In a series of studies on human subjects in the 1990s, Brennan et al. [120,125,126] showed that spinal manipulation but not sham manipulation nor soft tissue massage primed polymorphonuclear leukocytes (PMNs) and monocytes. Spinal manipulation enhanced the respiratory burst (a marker for phagocytic activity) of these white blood cells to a particulate challenge. The mechanism is unclear, although speculation on the role of substance P was discussed. Spinal manipulation also primed the polymorphonuclear leukocytes for enhanced production of cytokines as determined by the release of tumor necrosis factor in response to endotoxin challenge. The priming effect was short lived, being greater 15 minutes after manipulation compared with 30 and 45 minutes. The biological consequence of these changes have yet to be investigated, but their changes suggested their potential use, at least, as markers of successful spinal manipulation.

Conclusion

A theoretical framework has been presented for understanding the neurophysiological effects of spinal manipulation. The reasons underlying the biomechanical changes in the vertebral column are hypothesized to affect neural input, subsequently altering central processing and affecting reflex somatomotor or somatovisceral output. Table 2 summarizes the evidence for the theoretical relationships presented in this review. Spinal manipulation evokes changes in the neuromusculoskeletal system. The experimental evidence indicates that the impulse load of a spinal manipulation impacts proprioceptive primary afferent neurons from paraspinal tissues. In addition, spinal manipulation can affect pain processing, possibly by altering the central facilitated state of the spinal cord, and can affect the motor control system. Animal experiments show that sensory input from paraspinal tissues has the capacity to reflexively alter the neural outflow to the autonomic nervous system. However, the effects of spinal manipulation on the autonomic nervous system are less well investigated The neurophysiological evidence demonstrating physiological effects produced by spinal manipulation is growing. More than one mechanism likely explains the effects of spinal manipulation. During the past 10 to 20 years, novel experimental approaches have been developed to investigate both the effects of and the mechanisms underlying spinal manipulation. Neurophysiological studies of the spine using animal models are difficult, if for no other reason than the paraspinal tissues of interest directly overlie the central nervous system and the distances between paraspinal tissues and the spinal cord are short. Several experimental models have offered solutions to this difficulty. Continued work in this area will help us better understand the therapeutic mechanisms impacted through spinal manipulation.

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