



## Review

## Spinal manipulative therapy and somatosensory activation

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## ARTICLE INFO

## Keywords:

Spinal manipulation  
Neurophysiology  
Biomechanics

## ABSTRACT

Manually-applied movement and mobilization of body parts as a healing activity has been used for centuries. A relatively high velocity, low amplitude force applied to the vertebral column with therapeutic intent, referred to as spinal manipulative therapy (SMT), is one such activity. It is most commonly used by chiropractors, but other healthcare practitioners including osteopaths and physiotherapists also perform SMT. The mechanisms responsible for the therapeutic effects of SMT remain unclear. Early theories proposed that the nervous system mediates the effects of SMT. The goal of this article is to briefly update our knowledge regarding several physical characteristics of an applied SMT, and review what is known about the signaling characteristics of sensory neurons innervating the vertebral column in response to spinal manipulation. Based upon the experimental literature, we propose that SMT may produce a sustained change in the synaptic efficacy of central neurons by evoking a high frequency, bursting discharge from several types of dynamically-sensitive, mechanosensitive paraspinal primary afferent neurons.

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## 1. Introduction

Manually-applied movement and mobilization of body parts as a healing activity has been used for centuries (Wiese and Callender, 2005). A relatively high velocity, low amplitude force applied to the vertebral column with therapeutic intent, referred to as spinal manipulative therapy (SMT), is one such activity. It is most commonly used by chiropractors, but other healthcare practitioners including osteopaths and physiotherapists use it as well. Although SMT has been advocated for a wide range of health problems (Ernst and Gilbey, 2010), currently available best evidence suggests it has a therapeutic effect on people suffering some forms of acute neck and back pain particularly when it is used in combination with other therapies (Brønfort et al., 2004, 2010; Dagenais et al., 2010; Miller et al., 2010; Walker et al., 2010; Lau et al., 2011). Its effect on chronic low back pain is less clear (Rubinstein et al., 2011; Walker et al., 2010).

SMT is typically applied when dysfunctional areas of the vertebral column are found. Clinicians identify these areas based upon palpatory changes in the texture and tone of paraspinal soft tissues, the ability to elicit pain and/or tenderness from these tissues, asymmetries in hard or soft tissue landmarks, and restrictions in spinal joint motion (Kuchera and Kappler, 2002; Sportelli and

Tarola, 2005). The clinician's goal in applying a spinal manipulation is to restore normal motion and normalize physiology of the neuromusculoskeletal system in particular and potentially other physiological systems affected by the dysfunction.

The mechanisms responsible for the therapeutic effects of SMT remain unclear. Early theories proposed that the nervous system likely mediates the effects of SMT. For example, Korr (1975) proposed that SMT alters or modulates proprioceptive afferent inputs to the central nervous system. Twelve years later Gillette (1987) provided a speculative description of all afferent input likely to arise from SMT of the lumbar spine. The force–time profile of SMT, based upon the one study available at the time, was trapezoidal in shape, reaching a peak force of nearly 200 N and lasting nearly 400 ms before returning to pre-SMT levels. Identification of afferents likely activated by SMT was based upon a review of the experimental evidence describing the response characteristics of all known somatic mechanosensitive receptors to the mechanical features of the stimuli that activated them (e.g. force magnitude, rate of force application). Much of the data concerning receptor-type and response characteristics were derived from studies involving the appendicular somatosensory system since little was known at the time about the axial somatosensory system. Consequently Gillette's description (Gillette, 1987) provided a hypothetical profile of the afferent activity arising during SMT.

Since Gillette's (1987) benchmark paper, considerably more is known about the morphology of the vertebral column's somatosensory system (for example see Giles and Taylor, 1987; Richmond

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**Table 1**

Lists the receptors that have been identified in paravertebral tissues of the cervical (C), thoracic (T), lumbar (L), or coccygeal (Cx) regions of the vertebral column using morphological (M) or physiological (P) studies. The species in which the respective receptors have been studied is listed together with one reference to a study involving the species and study type.

Receptor	Region	Study type	Species	Evidence (see for example)
Muscle spindle	C	P	Cat	Richmond and Abrahams (1979)
		M	Cat	Richmond and Bakker (1982)
	C,T,L	M	Human	Boyd-Clark et al. (2002)
		M	Human	Amonoo-Kuofi (1983)
		P	Cat	Cao et al. (2009)
Golgi tendon organ	C	P	Cat	Richmond and Abrahams (1979)
		M	Cat	Richmond and Bakker (1982)
	L	M	Human	Mendel et al. (1992)
		M	Human	Roberts et al. (1995)
		M	Bovine	Roberts et al. (1995)
Paciform corpuscle	C	M		Richmond and Abrahams (1982)
				McLain (1994)
	L	M	Human Fetus	Jackson et al. (1966)
		M	Human	Jackson et al. (1966)
		M	Bovine	Roberts et al. (1995)
Ruffini ending	L	M	Human	Roberts et al. (1995)
			Human	Jiang et al. (1995)
Unencapsulated nerve endings	C	M	Human	Mendel et al. (1992)
			Human	Stilwell (1956)
	C,T,L	M	Human Fetus	Groen et al. (1990)
		M	Rat	Nakamura et al. (1996)
		M	Human Fetus	Jackson et al. (1966)
	L	M	Human	Jackson et al. (1966)
			Human	Jackson et al. (1966)

et al., 1988; Groen et al., 1990; McLain, 1994; Jiang et al., 1995; Bolton, 1998). Table 1 summarizes receptor types that have been found in paravertebral tissues. Similarly, more is now known about the mechanical characteristics of SMT. Additionally, *in vivo* and cadaveric studies have better informed us about the kinematics of vertebral motion segments produced by SMT. Together these new data provide a more informed basis for modeling SMT activation of the axial somatosensory system.

The goals of this article are to briefly update our knowledge regarding several physical characteristics of an applied SMT and to review what is known about the signaling characteristics of sensory neurons innervating the vertebral column in response to spinal manipulation. Then based upon this data, we describe neurophysiological events that may contribute to the therapeutic effects of spinal manipulation.

## 2. Physical characteristics of SMT

### 2.1. Mechanical parameters and forces associated with SMT

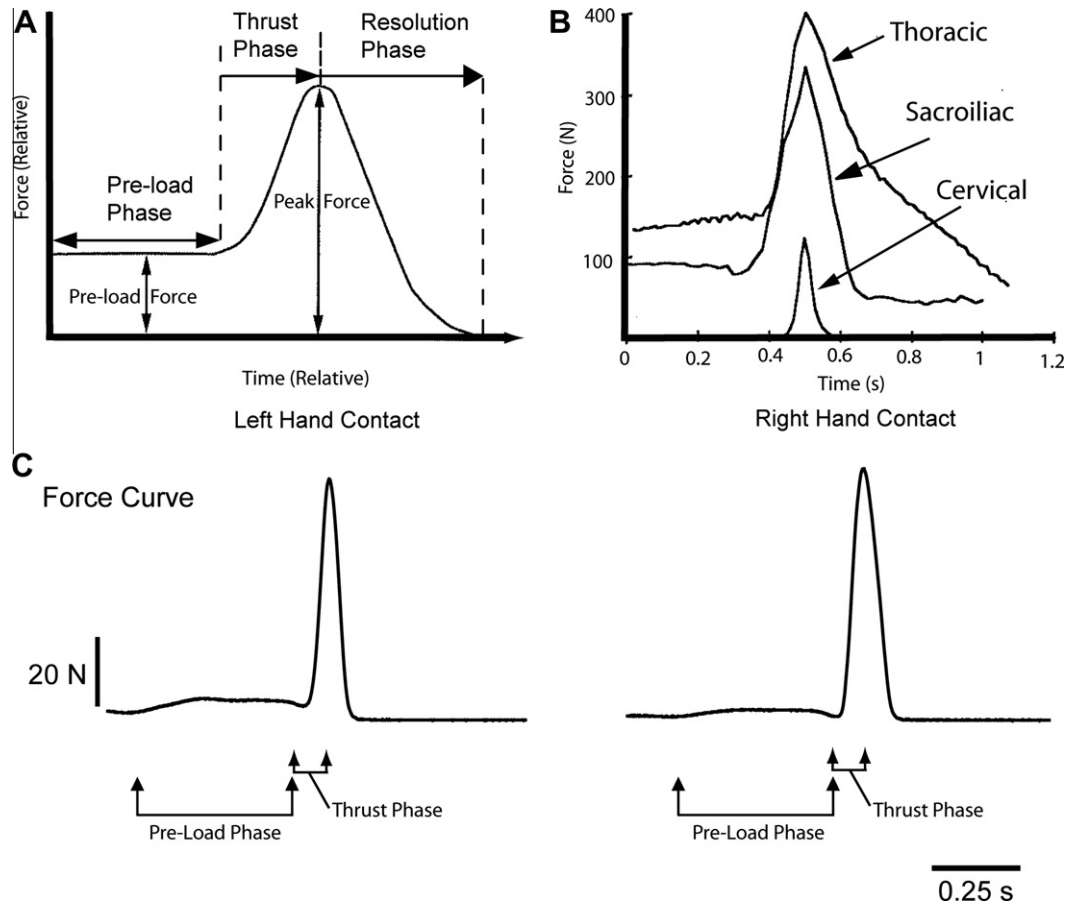
The biomechanical characteristics (i.e., force or displacement versus time curves) of a number of SMT techniques involving either manual or instrument-assisted protocols have been determined in studies performed directly on human subjects (for reviews see Lee et al., 2000; Herzog, 2010) or with the use of patient simulation devices (Kawchuk et al., 2006; Graham et al., 2010). Fig. 1 shows examples from both types of studies. As

described by Herzog (2010), the profiles may be characterized by a pre-load phase, a thrust phase which rapidly rises to a peak force, and a resolution phase (see Fig. 1A).

The characteristics of these profiles appear to vary depending upon region of the vertebral column to which they are applied (e.g. see Fig. 1B). In human studies the kinematic parameters of SMT have been obtained using a flexible force-sensitive mat interposed between the clinician's hands and the patient to record the force and duration of an SMT. SMT in the cervical region has relatively little pre-load ranging from 0 to 39.5 N (Herzog et al., 1993; Kawchuk et al., 1992; Kawchuk and Herzog, 1993). In contrast, the average pre-load forces during SMT in the thoracic region ( $139 \pm 46$  N,  $\pm$  SD) and sacroiliac region (mean  $88$  N  $\pm$  78 N) are substantially higher than in the cervical region and are potentially different from each other (Herzog et al., 1993). From the beginning of the thrust to end of the resolution phase, SMT duration varies between 90 and 120 ms (mean = 102 ms). The time to peak force during the thrust phase ranges from 30 to 65 ms (mean = 48 ms). Peak applied forces range from 99 to 140 N (mean = 118 N,  $n = 6$  treatments) (Herzog et al., 1993). In the same study with SMT directed at the thoracic (T4) region and applied to three different patients by the same practitioner, the mean (SD) time to peak force was  $150 \pm 77$  ms and mean peak force reached  $399 \pm 119$  N. During the resolution phase, force returned to pre-SMT levels over durations up to two times longer than that of the thrust phase. When SMT was applied to the sacroiliac joint, mean applied peak forces reached  $328 \pm 78$  N (Herzog et al., 1993), with the thrust and resolution phases having similar durations ( $\sim 100$  ms). The peak force during manipulation of the lumbar spine measured by Triano and Schultz (1997) tended to be higher than during the thoracic or sacroiliac manipulation measured by Herzog et al. (1993) and the force-time profiles resembled half-sine waves with the time to and from peak taking approximately 200 ms. Peak impulse forces during thoracic manipulation measured by Suter et al. (1994) approximated the  $>400$  N peak impulse force measured by Triano and Schultz (1997).

The physical characteristics of an SMT may vary based upon the technique being used and the individual practitioner. While instrument assisted SMT may apply preload forces on the order of 20 N, peak forces vary from approximately 50–380 N depending on the instrument being used and selection of the instrument's settings (Colloca et al., 2005). Up to 38% of the instrument assisted thrusts were reported to produce absolute forces significantly different ( $P \leq 0.05$ ) from each other (Kawchuk et al., 2006). In addition, the difference in applied force duration between two operators using instrument-assisted SMT can be as much as 75% (Kawchuk et al., 2006). Similarly, measurements of SMT forces and displacements applied to a non-biological device simulating the SMT's contact site also show variability. In a study measuring force and displacement over the duration of a toggle recoil SMT both force and displacement varied by 50% when performed by an individual practitioner while, between practitioners, force varied by up to 100% and displacement by up to 50% (Graham et al., 2010). These findings presumably identify practitioner-related variability since neither the instrument's nor the simulator's mechanical properties change. During a non-instrument-assisted, predominately rotatory manipulative procedure applied to the neck, practitioners did not consistently perform the procedure in that peak thrust velocities were different. However, better inter-practitioner than intra-practitioner consistency was observed for thrust duration (Ngan et al., 2005). Interestingly, a spinal mobilization (low velocity) manual technique (cervical lateral glide) performed on the neck demonstrated very small intra-practitioner variability (Vicenzino et al., 1999).

It is clear that the mechanical parameters of SMT vary significantly depending on the manipulated region of the vertebral column, the type of procedure being performed, and characteristics



**Fig. 1.** Force–time curves derived from high velocity, low amplitude spinal manipulations applied to humans (A and B) and to a simulation device (C). (A) Shows the phases and relative force occurring during the maneuver. Modified from Fig. 1, Herzog (2010). (B) Shows the mean force–time curves of manipulations applied to the cervical thoracic, and sacroiliac regions. Modified from Fig. 9, Herzog et al. (1993). (C) Shows the force–time curves of a toggle recoil manipulation performed with a left hand contact (left panel) and a right hand contact (right panel). Modified from Fig. 2, Graham et al. (2010).

of the individual practitioner. Nevertheless the force parameters are sufficiently described to allow modeling of the applied force to *in vivo* animal studies (see Section 3).

## 2.2. Vertebral motion with SMT

Less is known about the vertebral motion that occurs during SMT. Studies have been undertaken in unembalmed human cadavers to determine thoracic and lumbar vertebral motion induced by manual SMT. Absolute and relative linear (in mm) and angular (in degrees) vertebral motions have been studied in the thoracic spine (Gál et al., 1997a,b). Caudo-cranial and postero-anterior vertebral accelerations, and intra-intervertebral disc pressures have been studied in the lumbar spine (Maigne and Guillon, 2000). Although the number of subjects and datasets are small, these cadaveric studies indicate that vertebral kinematics following posterior to anterior thrusts involves biphasic and in some planes triphasic (pseudo-oscillatory) accelerations and rotations. Ianuzzi and Khalisa (2005a, 2005b) using an actuator to impose physiological rotations or simulated spinal manipulative loads to prosected human lumbar vertebral columns (T<sub>12</sub>–sacrum) investigated vertebral motion with 6 degrees of freedom. They demonstrated in the lumbar region that vertebral translation occurs primarily in the direction of the manipulative thrust and that vertebral rotations are relatively small (<2°). Interestingly they also found that strain in the facet joint capsule did not vary either from side to side or between capsules of vertebrae adjacent to the vertebra receiving the thrust. From this, they hypothesized that mechanosensitive afferents in

facet joint capsules both at the level of the applied thrust and at levels immediately adjacent would be activated.

Studies of vertebral motion associated with instrument-based SMT have been undertaken in anaesthetized humans (Keller et al., 2003) and sheep (Colloca et al., 2006; Keller et al., 2006a,b). More recently porcine prosected specimens of vertebral column were used to study vertebral motion (acceleration) occurring with instrument-induced SMT applied perpendicular and oblique to the SMT's contact area (Kawchuk and Perle, 2009). Together these studies indicate that instrument-delivered SMT thrusts induce transient oscillatory (lasting 100–150 ms), coupled (multiple axis) vertebral motions that vary depending on the subject being tested, and the location and magnitude of the applied force. The sheep preparation also demonstrates that, as might be expected, changing the force–time characteristics also changes the displacements and accelerations of both the target and adjacent vertebrae (Colloca et al., 2006; Keller et al., 2006a,b).

## 3. Studies of paravertebral somatosensory afferent activation during SMT-like motion

Despite the significant ethical and technical challenges, Colloca and colleagues performed electrophysiological recordings from the S1 nerve root and multifidus muscle in anaesthetized humans while simultaneously applying an instrument based SMT directed posterior to anterior in the lumbar region (Colloca et al., 2000, 2003; Keller et al., 2003). For the nerve root, they reported the occurrence of electrical activity with a mean onset latency ranging

from 8.2 to 10.7 ms following the thrust. For the multifidus muscle, they reported electromyographic activity (EMG) with a mean onset latency ranging from 5.5 to 18.3 ms. While these studies indicate nerve and muscle activity may be modulated by a spinal manipulative thrust, they provide limited information regarding the type of neurons affected or the neurophysiological mechanisms involved.

Two quite different *in vivo* experimental preparations using the anesthetized cat have been developed for investigating the neurophysiological effects of force–time or displacement–time profiles that simulate SMT when applied to the vertebral column. In one preparation defined angular motions can be imposed upon a cervical vertebra (Bolton and Holland, 1998). In the second preparation, defined loads can be applied to a lumbar vertebra under either force or displacement control (Pickar, 1999).

The first preparation has been used to emulate the force–time profile of an SMT's thrust phase by imposing rotational displacements of the C<sub>2</sub> vertebra about the neck's longitudinal axis (Bolton and Holland, 1998). Asymmetric tri-phasic (sine wave with dampened 2nd ½ cycle sine wave) displacements have also been used to emulate the acceleration profile and vertebral movements reported to occur during high velocity low amplitude thrusts in human cadavers (Gál et al., 1997a, 1997b) and during instrument based spinal manipulation (Keller et al., 2003). Simultaneous with the rotational displacements, electrophysiological recordings from ipsilateral or contralateral projecting primary afferents have been made.

The second preparation utilizing a computer-driven, feedback motor was first used to emulate the force–time profile of high velocity low amplitude manipulations given by clinicians to the lumbar spine (Pickar and Wheeler, 2001). Loads were applied at the L<sub>6</sub> spinous process (cat's have seven lumbar vertebrae) and directed cranially in the coronal plane using a ramp and hold (0.3 s) force profile representing the manipulation's pre-load phase followed by a force profile rising in 100 ms to a peak load of 100% of the cat's body weight representing the thrust phase. Simultaneously, electrophysiological recordings were obtained from individual primary afferents innervating the L<sub>6</sub> paraspinal tissues. In subsequent experiments, manipulative loads have been applied to the L<sub>6</sub> vertebra and directed ventrally in the transverse plane (Sung et al., 2005; Pickar and Kang, 2006; Pickar et al., 2007). Peak displacements of 1 and 2 mm and peak forces proportional to 33%, 66%, or 100% of the cat's bodyweight were used. The three forces induced L<sub>6</sub> displacements of 1.2 (±0.2), 2.0 (±0.5), and 3.3 (±1.1) mm, respectively. These displacements are comparable to the translation and rotational displacements (1.5 ± 0.5 mm and 2°–3.5°, respectively) occurring in human cadaveric lumbar spine when high velocity low amplitude thrusts are performed (Ianuzzi and Khalsa, 2005a).

### 3.1. Muscle spindle afferent responses

Activity of individual sensory neurons with a spontaneous resting discharge (15–98 impulses/s) have been studied during the application of spinal manipulative-like loads. (Pickar and Wheeler, 2001; Pickar and Kang, 2006; Pickar et al., 2007). Recordings were obtained from the L<sub>6</sub> dorsal rootlets. Afferents were identified as arising from muscle spindles located in lumbar multifidus or longissimus muscles on the basis of their receptive field's location, their responses to intra-arterial infusion of succinylcholine and/or to electrically-induced muscle twitch. The spindle afferents were further characterized as primary (group Ia) or secondary (group II) based upon their responses to ramp and hold movement of the L<sub>6</sub> vertebra. These studies have shown that the spinal manipulation's thrust phase significantly increases the discharge rate of muscle spindles in the deep lumbar paraspinal muscles (201 ± 57%) compared to the pre-load phase (29 ± 20%) (see Fig. 2A) (Pickar and Wheeler, 2001). Recovery of the spindle's firing rate following

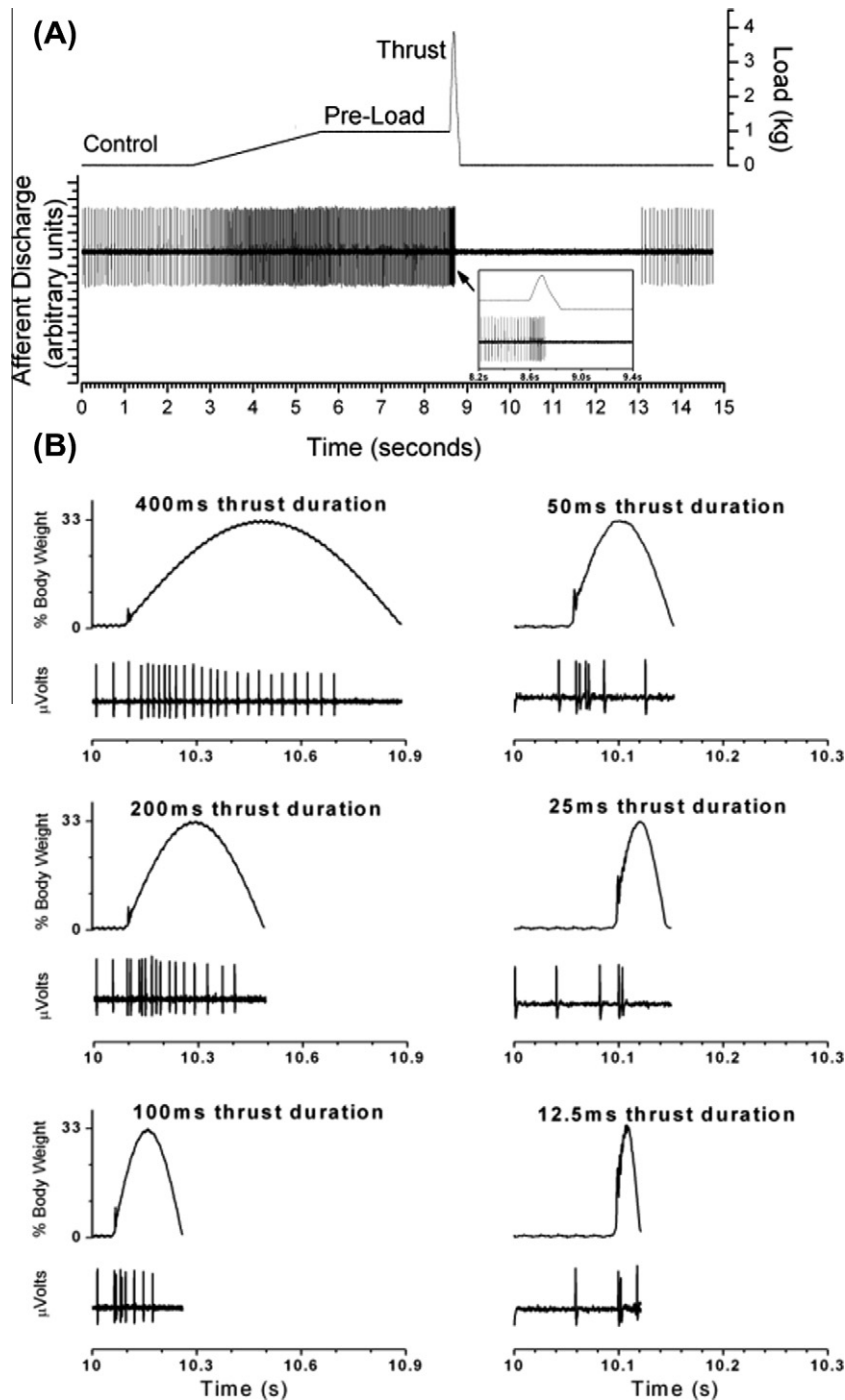
the resolution phase may be immediate or take some time (range 100 ms–21.2 s). Furthermore, changing the direction of the applied thrust changes the magnitude of the response.

Many afferents from muscle spindles in the lumbar region demonstrate a graded increase in mean instantaneous frequency when tested across a range of thrust phase durations from 12.5 to 400 ms (see Fig. 2B) (Pickar and Kang, 2006). In general, group Ia afferents appear more responsive to the spinal manipulative thrust than the group II spindle afferents. Some afferents exhibit an increase only at specific thrust durations. Discharge rate increases by 110–520 impulses/s during a 100 ms thrust duration whereas it only increases between 28 and 88 Hz impulses/s during a 800 ms thrust duration (Pickar and Kang, 2006). The graded increase in spindle discharge as thrust duration shortens (i.e., as the manipulation's speed becomes faster) is non-linear, with an inflection occurring at thrust durations less than 150 ms. This duration represents one that practitioners often achieve when applying a spinal manipulation clinically to either the lumbar or cervical region (see Section 2). The spindle's silent period following the resolution phase, which primarily occurs in group Ia afferents, becomes shorter as the duration of the impulse load becomes shorter. Group II spindle afferents do not become silent but it should be noted that their firing interval (inverse of the firing rate) is greater than the silent period of the group Ia afferents.

Afferent activity in cervical spinal nerves (dorsal rootlets) has been characterized as arising from neck muscle spindles on the basis of it being spontaneous, its receptive field location being confined to a single neck muscle, and an increase in its firing rate in response to an intra-arterial infusion of succinylcholine. However, in contrast to afferents innervating tissues of the low back, afferents innervating the neck are too short in the cat to allow accurate classification as groups I, II, III or IV on the basis of conduction velocity. Nevertheless, it has been possible to study putative muscle spindle activity in the cervical spine. As can be seen in Fig. 3, displacement of the C<sub>2</sub> vertebra can induce a decrease (Fig. 3A) or increase (Fig. 3B) in the spontaneous firing of a neck muscle spindle afferents depending on the direction of the displacement. Fig. 3 also shows that C<sub>2</sub> displacement can induce either an initial pause and then an increase (Fig. 3C) or an initial increase followed by a decrease (Fig. 3D) in spontaneous discharge. In each case, the spindle's spontaneous firing rate rapidly returns to the level of the pre-manipulative-like vertebral displacement.

### 3.2. Golgi tendon organ afferent responses

Afferents with receptive fields in lumbar paravertebral tissues of the cat were deemed to arise from Golgi tendon organs (GTO) if, (1) they did not exhibit spontaneous activity, but (2) responded to loads with short-lasting, low-frequency activity, (3) had irregular discharge rates in response to an intra-arterial injection of succinylcholine and, (4) had conduction velocities in the group I range (Pickar and Wheeler, 2001). These afferents exhibited responses to SMT-like loading quite different from that of muscle spindles. In particular, GTO afferents were rarely activated by the pre-load phase (with increases in firing rate by >10 Hz occurring on only 3 of 15 occasions) and were mildly activated by the thrust phase, increasing their firing frequency by only 21 ± 4 impulses/s during the thrust phase relative to the control and by only 19 ± 4 impulses/s relative to the pre-load phase. Also in contrast to muscle spindle afferents, GTOs responded even when the direction of the SMT was changed (cranial, caudal or 45° to the spine's long axis). With few exceptions GTO afferents became silent immediately following the thrust phase and they remained silent. In a second study using a manipulative-like load of 33% body weight (Sung et al., 2005), one putative GTO afferent showed a pattern of behavior similar to the muscle spindle afferents when tested over a range



**Fig. 2.** Lumbar paraspinal muscle spindle response to a high velocity, low amplitude spinal manipulative-like load. (A) Shows an original tracing of a spindle's response to the manipulation. Inset shows the spindle's discharge on an expanded time scale. (Adapted from Pickar and Wheeler (2001), with permission from Elsevier.) (B) Shows original tracings of a muscle spindle afferent's response to six different thrust durations (400, 200, 100, 50, 25, and 12.5 ms) using a half-sine waveform. (Adapted from, Pickar and Kang (2006), with permission from Elsevier.)

of thrust durations but its mean instantaneous firing rate during the thrust phase was substantially less than that of spindle afferents.

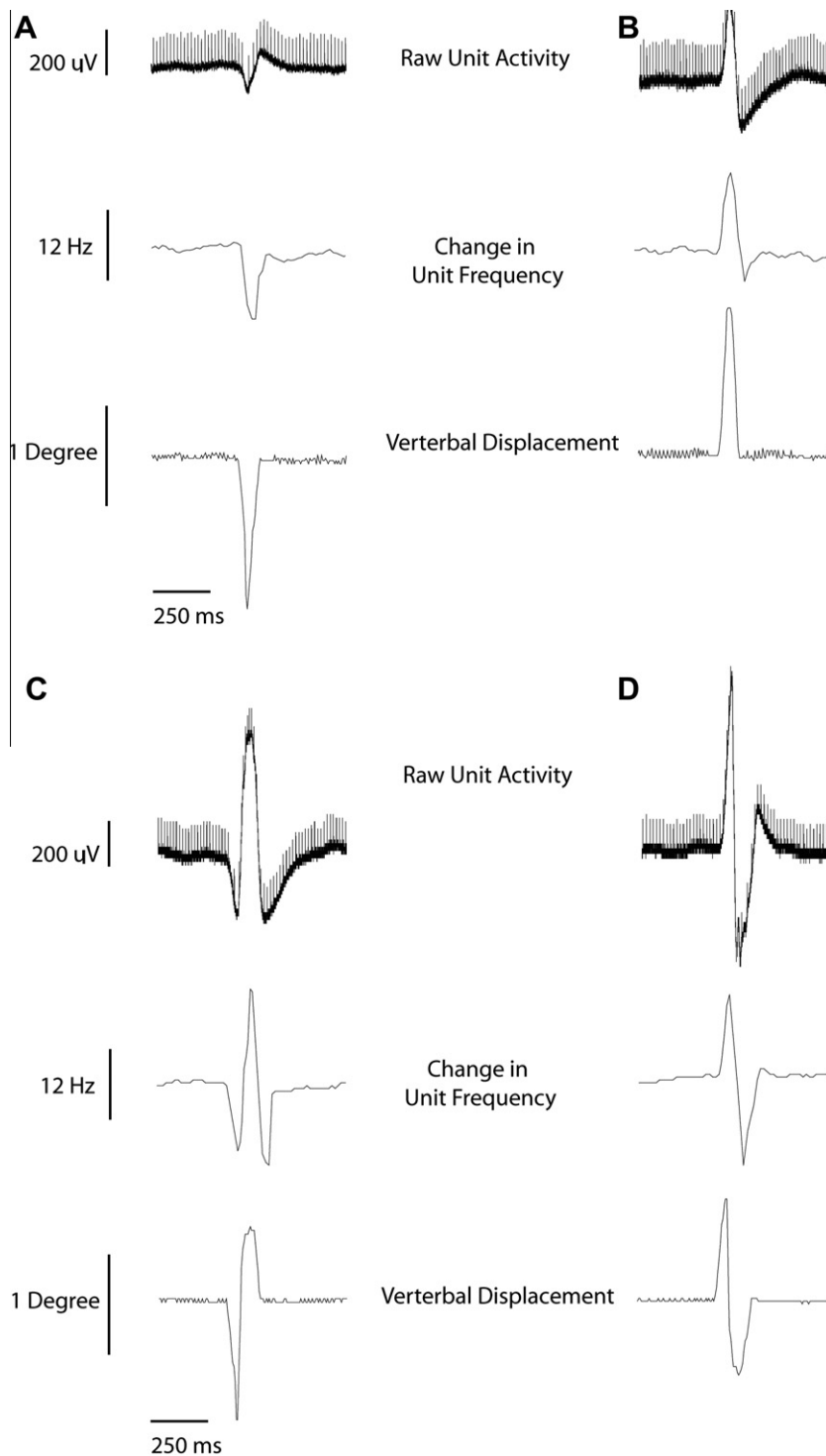
### 3.3. Putative Pacinian corpuscles afferents

Pickar and Wheeler (2001), reported the unique response of one afferent which was inactive at rest and rapidly adapted when the lumbar paraspinal tissues were probed. It responded to an SMT-like thrust (duration: 200 ms; peak force: 6.4 N) that distracted the facet joint, but it did not respond at loading rates  $\sim 10$  times

slower than the thrust rate nor with peak loads that were up to 4 times higher than the peak thrust force. If this afferent belonged to a GTO it would likely have been activated by the increasing load (Stuart et al., 1970). Because it responded to rate of mechanical loading, it was likely a Pacinian corpuscle (Sato, 1961).

### 3.4. Other afferents

Afferents from the cervical paravertebral tissues are difficult to accurately characterize because they cannot be identified on the



**Fig. 3.** Cervical muscle spindle afferent response to rapid rotation of the  $C_2$  vertebra simulating the thrust phase of a high velocity, low amplitude spinal manipulation. In each panel (A, B, C, and D) top trace shows an original recording of spindle activity, middle trace shows the instantaneous discharge frequency (bin width 0.125 s) and lower trace shows the  $C_2$  vertebra's relative position. (A) Shows a decrease in the muscle spindle afferent activity during the thrust and panel. (B) Shows an increase in its frequency during displacement to the right. The bottom two panels show a muscle spindle's response to vertebral displacement initially to the left and then right and back to the midline (C) and then with displacement initially to the right and then left and back to the midline (D). Note the (D) and (C) shift (movement artifact) in the tracing of the original muscle spindle recordings (Raw Unit Activity) is greater when the vertebra is displaced contralaterally to the short dorsal rootlet being recorded (Bolton PS, Holland CT. 1998 unpublished data).

basis of their conduction velocity and their receptive fields are difficult to isolate due to the extensive coupled movements of the cervical vertebra when mechanical forces are applied to determine mechanical thresholds. For example, Bolton and Holland

(1996) have noted that an afferent responding to a large mechanical force may not in fact represent a high threshold mechanoreceptor such as a GTO located at the site of the applied force, but represent a low threshold mechanoreceptor lying distantly and

responding to the dampened mechanical force. It has also been difficult to classify afferents that respond to movement of the C<sub>2</sub> vertebra but do not have spontaneous activity and do not respond to intra-arterial injection of succinylcholine (Bolton and Holland, 1996). In this study, some (2/8) afferents had receptive fields in the ipsilateral semispinalis cervicis or semispinalis dorsalis muscles and were activated during movements of the C<sub>2</sub> vertebra that lengthened these muscles but not when they were shortened. The responses were rapidly adapting, showing a burst of 3–5 spikes, suggesting they were afferents from either Golgi tendon organs or paciform corpuscles. However, this could not be confirmed. Interestingly, 75% of the afferents (6/8) were only activated by firm (noxious) pinching of the ipsilateral C<sub>2-3</sub> zygapophyseal joint capsule with half (3/6) demonstrating an after-discharge suggesting they conveyed nociceptive information.

### 3.5. Common features

It is clear from these studies in the lumbar and cervical regions that impulse loads with force time profiles similar to that of manually delivered high velocity low amplitude thrusts evoke a relatively high-frequency discharge from afferents innervating muscle spindles, GTO's and high threshold mechanoreceptors. There are currently no unequivocal data regarding whether SMT activates nociceptors.

## 4. Neurophysiological consequences of SMT that may underlie the effects of SMT

The biomechanical findings reviewed above indicate that the nature of the SMT thrust is a dynamic mechanical event. During the manipulation, tissue displacements and forces clearly change rapidly, with no static component, and last only a short time-interval. How could this dynamic, very short-lasting (<150 ms) mechanical stimulus change the behavior of the nervous system in a way that outlasts the intervention itself? The neurophysiological findings reviewed above provide an opportunity to consider a contributory mechanism. It has been suggested that a manipulation's potentially long-lasting influence on the nervous system can be regarded as a primary and/or secondary event (for example, Pickar, 2002; Leach, 2004; Henderson, 2005; Bialosky et al., 2009a). By primary we refer to any long-lasting neural response that arises as a direct consequence of the short-lasting neural activity that occurs during the manipulation. By secondary we refer to a long-lasting neural response that arises as a consequence of (i.e., secondary to) a long-lasting change in spinal biomechanics caused by the manipulation.

### 4.1. Spinal biomechanics (secondary events)

A number of sustained changes in spinal biomechanics have been hypothesized to occur as a result of SMT. For example, the impulsive thrust may alter segmental biomechanics by releasing trapped meniscoids, releasing adhesions, or by diminishing distortion in the intervertebral disc (Farfan, 1980; Giles, 1989; Lewit, 1991; Haldeman, 1978; Vernon, 1997). Also, individual motion segments are thought capable of buckling thereby producing relatively large vertebral motions that achieve a new position of stable equilibrium (Wilder et al., 1988). The manipulative impulse may provide sufficient energy to restore a buckled segment to a lower energy level thus reducing mechanical stress or strain on soft and hard spinal tissues (Triano, 2001).

Neural responses arising secondary to the long-lasting biomechanical changes may be broadly conceptualized as resulting from neurophysiological changes occurring at either the receptive endings of primary afferents and/or along transmission pathways

from these receptive endings. Mechanically-sensitive primary afferents with receptive endings embedded in deep paraspinal tissues respond to mechanical stresses and strains in their local environment (Iannuzzi and Khalsa, 2005a). Long-lasting changes in their mechanical environment could modify the mechanosensory information received by the spinal cord and brain. Signals from chemoreceptors may also be altered to the extent that inflammatory conditions are altered by the manipulation (e.g. see Song et al., 2006). Transmission pathways on the other hand include both peripheral nerves and ganglia where they pass through or lie in the intervertebral foramen, and the spinal cord and brainstem where the latter extends through the foramen magnum into the neural canal. Sustained compressive force on neural tissue at these sites is thought to affect both impulse-based activity (action potential frequency) and non-impulse-based activity (axoplasmic transport) (see Korr, 1978). It has been hypothesized that spinal manipulation can relieve mechanical compression on these transmission pathways and induce beneficial changes in the chemical milieu of these neurons (see Leach, 2004; Henderson, 2005 for a more thorough discussion of this topic).

### 4.2. Activation of somatosensory receptors (primary events)

Gillette (1987) proposed that spinal manipulation activates all known mechanosensitive, somatosensory receptors because they all possess mechanical thresholds lower than the peak force delivered during a manipulation and because the 40 *in toto* receptor-types are responsive to dynamic and/or static components of a mechanical stimulus. The rationale was based upon the one load-time profile for a spinal manipulation that had been recorded at that time (see Gillette, 1987). More recent biomechanical data (see Section 2) indicate a revision to this load-time profile is needed. A high-velocity, low amplitude spinal manipulation, which over 90% of chiropractic patients receive as part of their care (Christensen et al., 2005), is purely dynamic, with a short rise-time to its peak amplitude, and with no static component (see Fig. 1). Based upon these features, the proposed receptor population responsive to a spinal manipulation can be reduced by more than half, to only those that have a substantial dynamic component. Thresholds of these afferents are less than 20–30 N (see Table 2 of Gillette, 1987), and represent magnitudes less than a manipulation's peak force. Thus, all four classes of primary afferents neurons, [group Ia, Ib, and II(A $\beta$ ), III(A $\delta$ ) IV(C) fibers] would be expected to respond during the manipulation. However, vertebral tissues could act as low-pass mechanical filters, reducing the stimulus's dynamic component. In the extreme, the applied load may dissipate and its magnitude become insufficient to activate these sensory receptors. Nevertheless, recordings of multi-unit and single-unit activity in paraspinal primary afferents show that spinal manipulation does indeed stimulate paraspinal afferents (see Section 3).

To date, only muscle spindle afferents in the low back have been systematically studied and their response to spinal manipulation characterized (see Section 3.1). Their non-linear behavior in response to the duration of the manipulation's thrust phase might not be considered surprising based upon the long-known velocity sensitivity of spindles studied in limb muscles. Like limb muscle spindle afferents (e.g. see Fig. 10 in Matthews (1963)), paravertebral group Ia spindle endings show a response inflection. This inflection represents a threshold for higher spindle discharge frequencies than would otherwise be predicted from their discharge frequencies evoked by slower stretch rates. Most interestingly, this threshold stretch rate ( $\sim$ 10 mm/s) is comparable to the rate at which a spinal manipulation imparts movement to a vertebra, translating it less than 3 mm in less than 150 ms (see Section 2.2).

Muscle spindles also demonstrate another type of dynamic threshold when their sensitivity has been studied using sinusoidal stretch–shortening cycles. In the limbs, both group Ia and II muscle spindle afferents show a non-linear increase in sensitivity at sinusoidal loading rates of 1.5 cycles/s (e.g. see Fig. 5 in Matthews and Stein (1969)). It can be seen in Fig. 2B that when a spinal manipulation is modeled as a half-sine wave the manipulative thrust represents one-quarter cycle. A thrust duration of 150 ms would represent a loading rate of 6.7 cycles/s and would be faster than the sinusoidal rate threshold for augmented spindle sensitivity. Together, these findings suggest that one consequence of a spinal manipulation is that it creates a higher frequency sensory input from muscle spindles than otherwise occurs during daily spinal motion. The sensory barrage from the population would be relatively synchronous in time, occurring over the time interval of the thrust (<150 ms) and vertebral motion that accompanies it. The sensory inputs would likely arrive at the central nervous system from a relatively localized area of the spine (see Section 2.2).

By comparison with muscle spindles, the relationship between the velocity of an applied mechanical stimulus and the discharge pattern of mechanosensitive, non-spindle afferents in either the vertebral column or the limbs is virtually unknown. For example in the finger, Edin et al. (1995) showed that discharge rates of dynamically-sensitive, cutaneous group II mechanoreceptors increased as the velocity of skin indentation increased. The formal relationship between the two was not characterized. Similarly, A- $\delta$  and C-fiber mechanonociceptors are known to fire an initial high burst during a dynamic mechanical stimulus application (Mense, 1986; White and Levine, 1991) but how the duration of their discharge frequency is formally related to either the magnitude or velocity of the stimulus is not known. If paraspinal non-spindle afferents are also activated by a spinal manipulation (see Section 3.4), it seems reasonable to think that they too present a burst of high frequency activity to the central nervous in a synchronous manner and from a localized area of the spine.

Knowledge that SMT-like movements produce a short-lasting, high frequency barrage of action potentials (see above) raises the possibility that SMT may induce longer term effects by modulating the central nervous system. Nearly, three decades ago studies showed that synaptic efficacy is affected by the history of high frequency bursting from group Ia and II muscle afferents (Davis et al., 1985; Luscher et al., 1983; Collins et al., 1984). The effect lasted beyond the duration of the burst itself. In  $\alpha$ -motoneurons, bursts of action potentials with short interspike intervals affected the magnitude of post-synaptic potentials differently from longer interspike intervals. In addition,  $\alpha$ -motoneurons are bi-stable and can sustain plateau potentials. Brief periods of excitation can switch them into a period of self-sustained firing (Hounsgaard et al., 1986). Such a state appears to have consequences for the normal production of muscle force (Collins et al., 2002). Such processes may underlie experimental findings showing changes in parameters related to increased muscle excitability following SMT (Suter et al., 2000; Dishman et al., 2002; Keller and Colloca, 2000; Koppenhaver et al., 2011).

High frequency stimulation of small diameter A- $\delta$  and C-fibers also affects synaptic efficacy. Both long-term potentiation as well as depression have been produced (Randic et al., 1993). The change in behavior of second order neurons lasts up to 1 h following the initial sensory barrage (Randic et al., 1993; Ikeda et al., 2000). In these experiments, a peripheral nerve was electrically stimulated thereby synchronously activating the afferent population. The whole nerve was stimulated at 100 Hz over a short lasting interval (~1 s) and was given several times at ~10 s intervals. The physiological relevance of such a stimulus has been questioned because C- and perhaps A- $\delta$  fibers do not typically discharge at such high rates, but stimulation using more intermediate frequencies

(20 Hz) also produces long-lasting changes (3–6 h) in synaptic efficacy (Liu and Sandkühler, 1997). The stimulus durations are clearly longer than a manipulative stimulus (<150 ms) however, we currently lack knowledge regarding how short a duration is capable of eliciting a change in synaptic efficacy. In addition, it is not known what discharge rates are evoked in paraspinal C- and A- $\delta$  fibers by spinal manipulation.

While changes in synaptic efficacy produced by high frequency stimulation paradigms have typically been applied toward understanding cellular mechanisms underlying hyperalgesia (Sandkühler, 2009), the findings may also provide a reasonable basis for considering how the short-lasting, dynamic mechanical input of a spinal manipulation produces a neural response that outlasts the intervention itself. This neurophysiological process may underlie findings from clinically-oriented basic science studies showing that spinal manipulation reduces temporal summation of thermal stimuli delivered to the periphery (George et al., 2006; Bialosky et al., 2009b; Bishop et al., 2011).

## 5. Conclusion

In conclusion, spinal manipulation could affect the nervous system by activating paraspinal sensory neurons during the maneuver itself and/or by altering spinal biomechanics. Biomechanical changes which follow the manipulation would, in turn, modulate paravertebral sensory neuron signals. As a short-lasting, dynamic mechanical stimulus, spinal manipulation may take advantage of two signaling characteristics of the nervous system: (1) inherent high frequency signaling properties of dynamically-sensitive primary afferent neurons and (2) response properties of post-synaptic neurons. Experimental studies reveal that spinal manipulation evokes a high frequency discharge in some primary afferents. In experimental studies not using spinal manipulation, spatial and/or temporal summation of high frequency input produces sustained changes in synaptic efficacy. Future studies directed at understanding how central neurons are affected by high frequency sensory input from paraspinal tissues during the manipulation are warranted based upon the literature and should contribute to our understanding of the mechanisms for spinal manipulation's action.

## Conflict of interest

J.G. Pickar and P.S. Bolton have no conflicts of interest.

## Acknowledgments

J.G. Pickar's research is supported by Grants from the National Center for Complementary and Alternative Medicine (NCCAM). Some investigations were conducted in a facility constructed with support from Research Facilities Improvement Grant No. C06 RR15433 from the National Center for Research Resources, National Institute of Health.

P.S. Bolton's research is supported by Grants from the National Health and Medical Research Council of Australia and the Australian Spinal Research Foundation.

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