Peripheral Proprioceptive and Central Nociceptive Responses to Spinal Manipulation Dosage Parameters

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PROPRIOCEPTIVE RESPONSES

Aberrant neuromuscular control of the trunk along with the inability of individuals with low back pain (LBP) to adopt optimal postural control strategies are thought to be involved in the etiology of LBP.[1,2] Patients with LBP have shown a variety of sensorimotor abnormalities including abnormal reflex responses characterized by reduced reflex gain and slowed reaction latencies, impaired lumbosacral proprioceptive acuity, dysfunction in trunk muscle response and control, altered postural balance strategies, higher spinal loads during highly controlled exertions and intervertebral joint dysfunction.[3-6] Many of these abnormalities are consistent with alterations in sensory feedback from the paraspinal muscle spindles which have been shown to have 5-10x more dynamic responsiveness than appendicular muscles.[7] Spindles in paraspinal muscles provide the central nervous system with sensory information regarding changes in muscle length and shortening velocity and thus are the proprioceptors most likely reporting changes in intervertebral position and aberrant vertebra movement.

Spinal manipulation is a commonly used non-pharmacologic therapeutic intervention considered clinically effective for the treatment of neck and low back pain. Mechanical loading profiles measured during a clinically delivered High Velocity Low Amplitude spinal manipulation (HVLA-SM) indicate that the thrust phase of a spinal manipulation can be likened to the up-ramp of a triangle wave.[8] Peak manipulative forces during clinical treatment of the lumbosacral region can range from 200 to 1600 N with a time to peak force being <150 ms.[8-9] Clinician-controlled biomechanical HVLA-SM parameters such as thrust magnitude, thrust duration, and tissue preload are thought to be critical to clinical expertise as well as to contribute to therapeutic efficacy of spinal manipulation. It therefore becomes crucial to understand how these HVLA-SM biomechanical parameters affect both peripheral and central neuron responsiveness.

Increasing evidence for proprioceptive-related changes in individuals with LBP combined with the possible relationship between biomechanical parameters and its clinical success for LBP, motivated a series of basic science investigations to determine the relationships between biomechanical parameters of simulated HVLA-SM and mechanoreceptor activity from muscle spindles in the low back in a cat preparation.

General Methods & Results

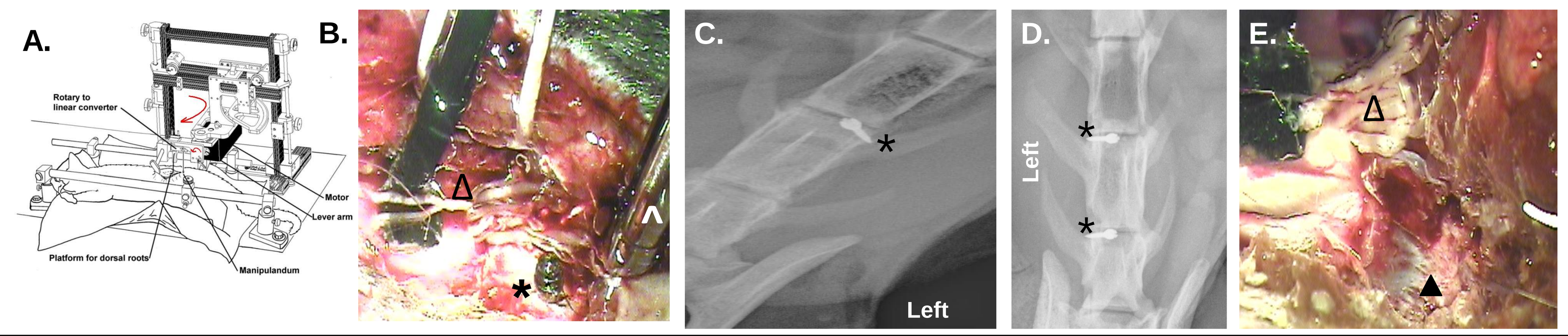


Fig. 1 Schematic (A), photographs (B, E) and x-rays (C, D) of the experimental cat preparation. (*) 10mm dental implant screw, (^) forceps attached to L_6 spinous process, (Δ) L_6 dorsal rootlets, (▲) facetectomy.

Neurophysiological Recordings from Muscle Spindles in the Back:

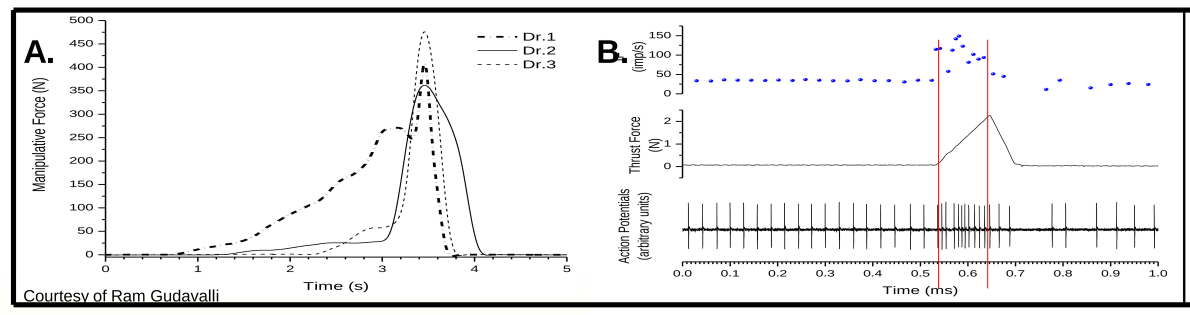
- Single unit activity from longissimus or multifidus muscle spindles was recorded from L_6 dorsal roots of deeply anesthetized (Nembutal) adult cats.
- Afferent spindle activity was confirmed based upon decreased discharge to electrically-induced muscle contraction and increased discharge to vibration (90Hz) and succinylcholine (i.a. 100-200ug/kg).
- Spindle discharge was first quantified as instantaneous discharge frequency (IF). Mean IF (MIF) was calculated during the HVLA-SM and over 2 seconds preceding it. Results are presented as the difference in MIF (ΔMIF) by subtracting MIF during from MIF preceding the SM.

Spinal Manipulation:

- Paraspinal tissues remained intact from L_6 caudalward in most preparations. Multiple screw preparations required that the skin be incised caudal to L_7.
- Spinal manipulation was applied either through a pair of forceps clamped onto the L_6 spinous process or through a custom-made polymer tips applied to the intact dorsal skin over the L_6 spinous process.
- HVLA-SM was delivered using a computer-controlled electronic feedback motor with peak forces of 25, 55, 85, or 100% of an average cat's body weight (3.95 kg), or peak thrust displacments of 1, 2, or 3 mm, and thrust durations between 75 and 250ms in the posterior-to-anterior direction (Figs. 1A, 2B).

Establishing Changes in Segmental Stiffness:

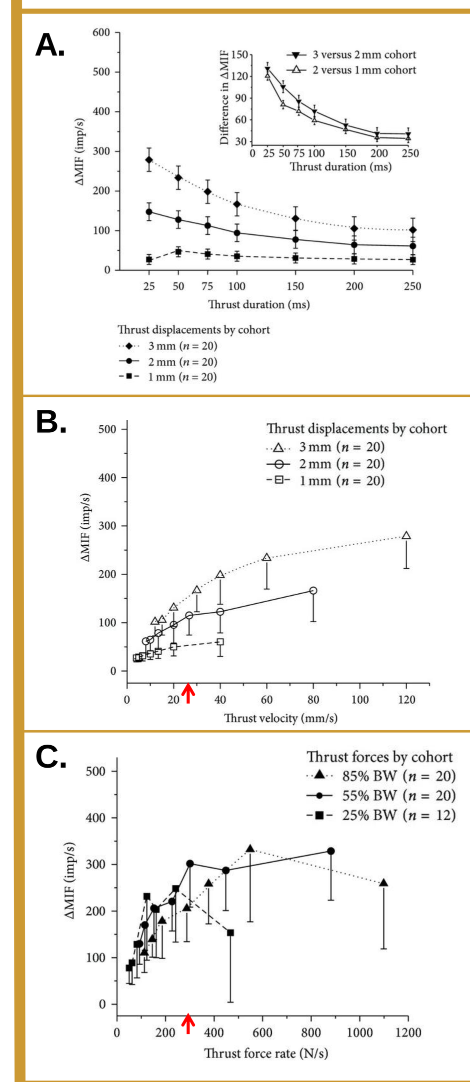
- Increased joint stiffness was created by placing a 10mm dental implant screw unilaterally through the left L_5/L_6 facet joint (Fig. 1C), the left L_5/L_6 and L_6/L_7 facet joints (Fig. 1D), or the left L_4/L_5, L_5/L_6, L_6/L_7 facet joints (not shown). The right paraspinal muscles remained intact in all preparations.
- Decreased joint stiffness was created by performing a unilateral (left) facetectomy of the L_5/L_6 joint.
- Forces and displacements applied at the L_6 spinous process were simultaneously measured from outputs of the control system. The slope of the most linear portion of the force-displacement curve was calculated either from a 1mm ramp movement representing pre-manipulation spinal joint stiffness for each joint condition (laminectomy-only, laminectomy & fixation, laminectomy & facetectomy) or during the HVLA-SM thrust from thrust onset for each joint condition.
- Preparations with at least 4% change (increase or decrease) in joint stiffness compared to the laminectomy-only condition were analyzed.



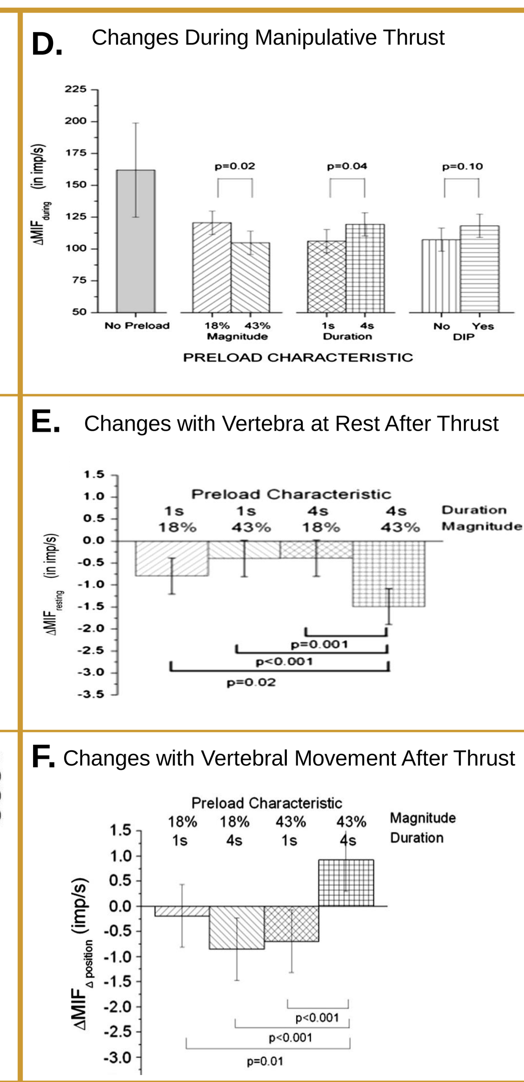
Courtesy of Ram Gudavalli

Fig. 2 (A) Force-time profiles from three doctors of chiropractic delivering an HVLA-SM. Note the similarities and differences in biomechanical parameters. Optimal HVLA-SM parameters are unknown. (B) An example of a simulated HVLA-SM (without pre-load) along with lumbar muscle spindle primary afferent response during and following the HVLA-SM.

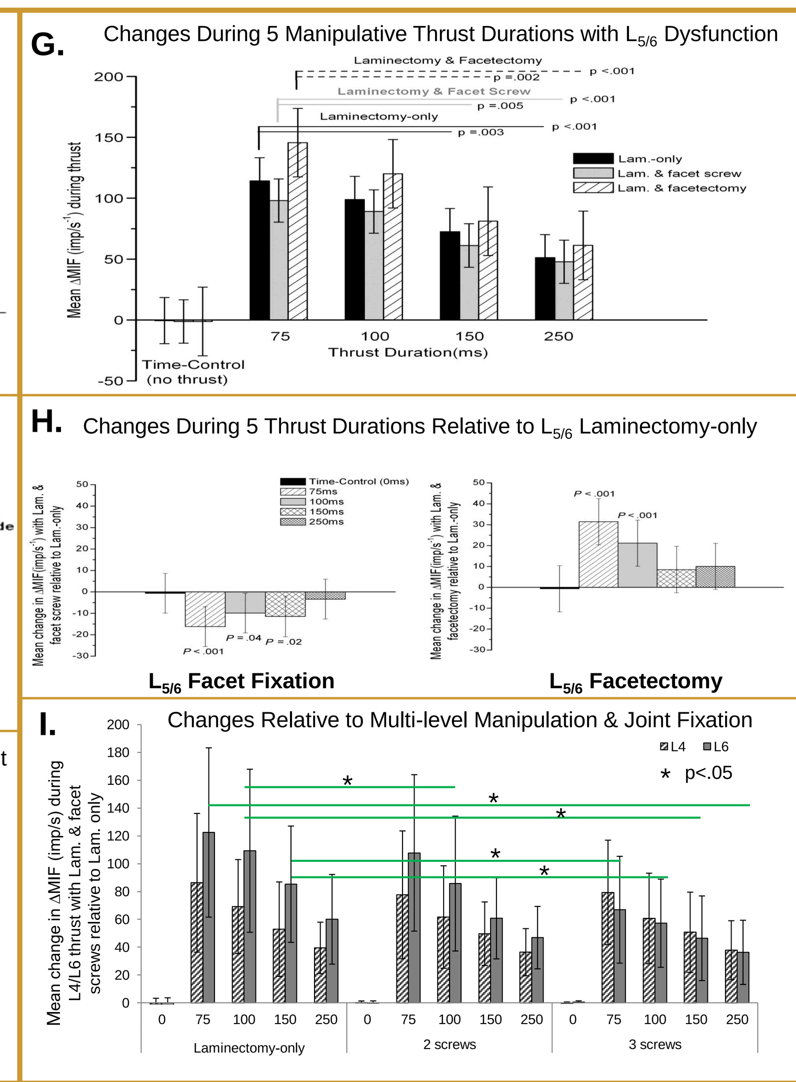
Thrust Parameters	Preload Parameters	Effects with Joint Dysfunction



Relationship between spindle discharge during a manipulative thrust and (A) thrust duration, (B) thrust velocity, (C) thrust force rate under either displacement or force control. Note plateau effect[↑]. Symbols represent average for cohort. Error bars represent 95% confidence intervals (CI).[10]



Effect of preload characteristics on muscle spindle discharge during (D) or following (E, F) the manipulative thrust (means and 95% CIs). Interactions between preload magnitude and duration are shown.[11]



Comparisons between mean change in MIF (ΔMIF) during 5 manipulative thrust durations applied in each of 3 spinal joint conditions (G) as well as relative to laminectomy-only (H) in a model of single $L_{5/6}$ joint dysfunction. Comparisons between ΔMIF during 5 manipulative thrust durations applied at either L_4 or L_6 spinous in the presence of multi-level ($L_{5/6}$, $L_{6/7}$, $L_{4/5}$) joint dysfunction(I). Data shown as means and 95% CI.[12]

NOCICEPTIVE RESPONSES

High velocity low amplitude spinal manipulation is a commonly used non-pharmacological mind/body intervention clinically shown to increase mechanical and thermal pain thresholds (i.e. decrease pain sensitivity) in areas distant from treatment sites in both asymptomatic and symptomatic individuals.[12] These findings suggest that HVLA-SM alters processing of afferent nociceptive input at central levels. Optimizing biomechanical parameters that characterize a spinal manipulation such as thrust magnitude, thrust duration, loading direction relative to the patient, and tissue pre-load are thought to be critical to clinical expertise and/or clinical efficacy. The thalamus is a key subcortical modulatory site that processes ascending innocuous as well as noxious somatosensory input from the periphery. The ability of the thalamus to modulate ascending sensory input as well as interact functionally with descending pain modulating structures such as the periaqueductal gray (PAG) is not well understood despite studies showing the existence of direct projections between multiple thalamic nuclei and the PAG.[13] Recently in humans it was demonstrated that the lateral thalamus and PAG interact reciprocally at short latencies (~5ms) and that stimulation of either structure relieved pain to various degrees.[15] Although more work in this area is required, the authors suggested that the thalamus and PAG influence each other via a fairly direct pathway not involving spinal cord circuitry and are thereby important in pain perception.[15] Whether or not such a pathway or other pathways involving the thalamus could ultimately contribute to the immediate and widespread hypoalgesia following HVLA-SM is plausible but speculative at this point.

General Methods & Results

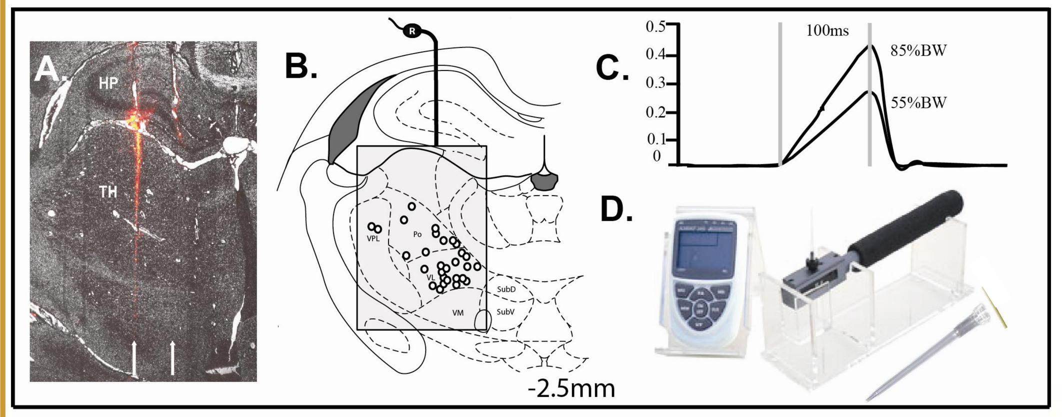


Fig. 3 (A) An example of DiI electrode tracks through the lateral thalamus (TH) hippocampus (HP). (B) A schematic showing the location of 29/47 thalamic neurons responding to mechanical stimulation of the trunk at -2.5mm caudal from bregma (posterior (Po), Submedius (SubD, Sub V), ventrolateral (VL), ventrolateral posterior (VPL). The remaining 18/47 neurons are located at adjacent levels. (C) Force profiles for L5 spinal manipulation thrust with 100ms duration at 55% and 85% of rat body weight (BW). (D) Photograph of the electronic von Frey (IITC-Model 2390) accompanied with a rigid tip used to determine mechanically evoked response thresholds in the trunk.

Lateral Thalamic Extracellular Recordings:

- For electrophysiological recordings, adult male Wistar rats were anesthetized with an intraperitoneal injection of 50% urethane (1.2g/kg) and maintained with supplement doses (5% urethane) administered intravenously as needed. Activity in lateral thalamic neurons was recorded extracellularly with DiI (1,1'-dioctabecyl-3,3,3',3'-tetramethyl-indocarbocyanine perchlorate)-coated tungsten microelectrodes having 6 - 8 MΩ impedance (**Fig. 3**) Thalamic electrode tracks were between -2.04 and -3.30mm caudal to bregma and 1.2 and 3.8mm lateral to midline. Neurons with receptive fields including the dorsolateral trunk were characterized using graded mechanical stimuli (gentle stroking with a nylon brush and noxious pinch with a serrated forceps). Neurons responding to innocuous stroking and noxious pinch in a graded fashion were classified as WDR whereas neurons responding only to trunk pinch were classified as NS.

Spinal Manipulation:

- A computer controlled electronic feedback system was used to deliver a linearly increasing dorsal-ventral HVLA-SM thrust force with a peak amplitude of 55% or 85% rat body weight over a duration of 100ms (**Fig. 3C**). A time-control (0 ms thrust duration, i.e. no thrust force) was included from which potential spontaneous changes in thalamic mechanical responsiveness could be determined. Contact for the HVLA-SM thrust was made by forceps rigidly attached to the L_5 spinous process. HVLA-SMs were separated by 5 minute intervals.

Mechanical Activation Threshold

- Once a thalamic neuron responsive to trunk stimulation was located, an electronic von Frey anesthesiometer (with a rigid tip adapter for deep pressure; 0.79mm² contact area) (**Fig. 3D**) was used to apply mechanical stimuli (measured in grams) in each of three directions on the dorsum of the trunk: dorsal-ventral, 45˚caudalward and 45˚cranialward. Electronic von Frey trunk stimuli were applied within 2 cm of the spine.

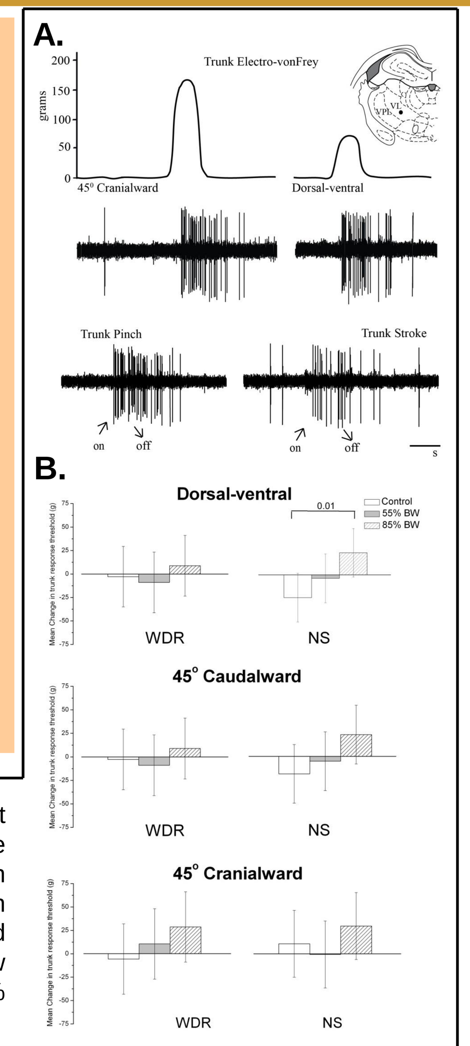


Fig. 4. (A) Responses of a single wide dynamic range thalamic neuron located (•) in the ventral lateral (VL) nucleus at -2.5mm caudal to bregma (upper row). Raw electrophysiological responses to lumbar trunk electronic von Frey stimuli (middle row) in the 45⁰ cranialward (161g) and dorsal-ventral direction (69g). Note graded response to trunk stroke and trunk pinch (lower row). Cal bar = 1s. (B) Mean changes following HVLA-SM in lumbar trunk electronic von Frey mechanical activation response thresholds (grams) for the dorsal-ventral, 45° caudal and 45° cranial directions of wide dynamic range (WDR) and nociceptive specific (NS) lateral thalamic neurons following time-control, 55% and 85% body weight high velocity low amplitude spinal manipulation thrust duration. Data are reported as means and 95% confidence intervals (lower, upper 95% CI).[16]

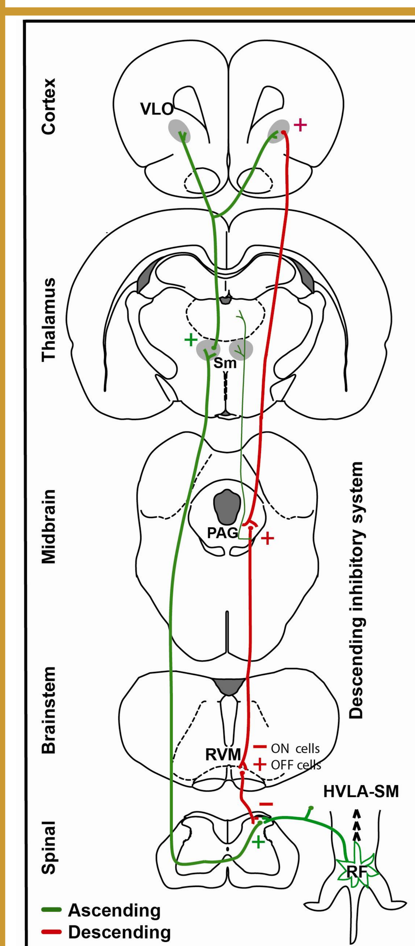
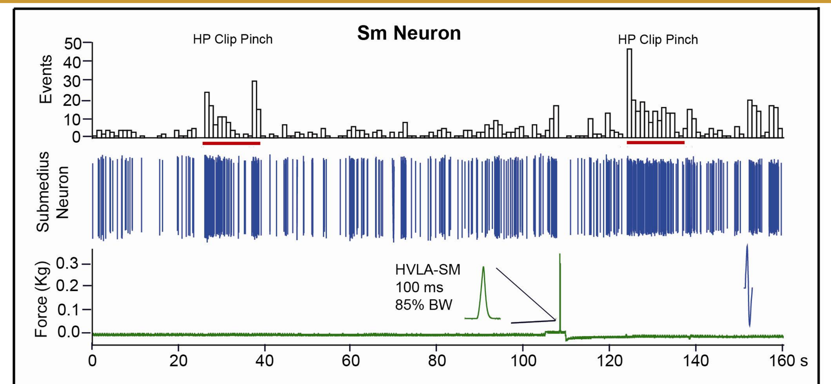


Diagram of proposed pain modulatory feedback loop of body-based manual therapies including high velocity low amplitude spinal manipulation (HVLA-SM). The feedback loop consists of the spinal cord dorsal horn-thalamic nuclei (submedius; Sm)-ventrolateral orbital cortex (VLO)-periaqueductal gray (PAG)-rostral ventromedial medulla (RVM)-spinal cord dorsal horn. +, excitation; -, inhibition, RF, receptive field.



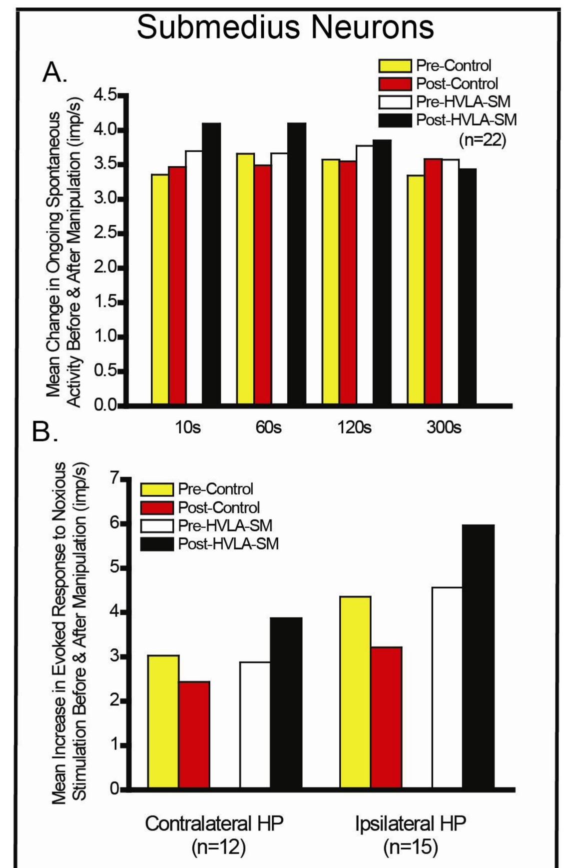
Shows an example of a left thalamic submedius neuron excited by noxious stimulation (small arterial clip) applied to the right hindpaw (HP) prior to and 10-15s following a HVLA-SM of 85% body weight (BW) and 100 ms thrust duration. There was an increase in the post-HVLA evoked response compared to control.

Thalamic Submedius Nucleus Recordings

Anatomical studies have established that the submedius (Sm) receives major projections from both the medulla and spinal cord dorsal horn neurons.[16] As one of the initial subcortical relays, the Sm has been implicated in the central mechanisms of acupuncture via a feedback loop involving the spinal cord (SC) dorsal horn→thalamic Sm→ ventrolateral orbital cortex (VLO)→periaqueductal gray (PAG)→rostral ventromedial medulla (RVM)→SC dorsal horn.[18,19] A study is currently being conducted to determine whether HVLA-SM alters neural activity in this initial subcortical relay of the thalamic Sm nucleus relative to noxious hindpaw stimulation (small arterial clip).

Preliminary Results:

Spontaneous thalamic Sm activity may increase for a period of at least 60s following HVLA-SM (black bars in Fig. A to the right). In addition, in those thalamic Sm neurons classified as being responsive to noxious stimuli (neurons exhibiting at least a 15% change in discharge following application of the noxious stimulus) HVLA-SM appeared to increase their response to noxious stimulation (black bars in Fig. B to the right).



Pilot Data. (A) The mean change in spontaneous activity (imp/s) of thalamic submedius (Sm) neurons over 4 time durations before and after control or HVLA spinal manipulation, (B) Mean increase in evoked response to noxious stimulation (small arterial clip) applied to the rat hindpaw (HP) contralateral or ipsilateral to Sm extracellular recording.

CONCLUSIONS

As an HVLA-SM's thrust duration approaches those used clinically (≤ 100ms) the neural discharge frequency of paraspinal muscle spindle afferents increases in a non-linear fashion regardless of the presence of spinal joint dysfunction. HVLA-SM thrust velocities greater than 20-30 mm/s and thrust rates greater than 300 N/S tend to maximize this peripheral sensory input. Tissue pre-load applied prior to the HVLA-SM thrust also impacts the discharge of paraspinal spindles during manipulation itself.

Preliminary findings suggest that a minimum thrust magnitude may be required to elicit an HVLA-SM induced hypoalgesic effect and that HVLA-SM increases ongoing spontaneous thalamic neuron activity as well as increased thalamic response to noxious mechanically-evoked stimulation.

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