Effect of Spinal Manipulation Thrust Duration on Trunk Mechanical Activation Thresholds of Nociceptive-Specific Lateral Thalamic Neurons

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Introduction

Spinal manipulation has been shown to be effective in treating neck and low back pain. The neurophysiological mechanisms by which this occurs remain elusive. Experimental efforts to better understand the neural effects of spinal manipulation at different levels of central ascending and descending nociceptive processing are needed to help elucidate the central mechanisms responsible for the near immediate hypoalgesic effects following spinal manipulation. Moreover, little is known about which clinician-controlled mechanical parameters could potentially optimize spinal manipulation-induced hypoalgesia including: magnitude and/or duration of preload, manipulation magnitude, manipulation duration and the consequent thrust rate, contact point and/or loading direction relative to patient position.

While some convergence and modulation of primary afferent input is known to occur at the level of the spinal cord, neuroimaging studies in animals have demonstrated decreased activation in supraspinal structures involved in pain processing following manual therapy intervention. The thalamus is a supraspinal structure that has long been known to have discriminatory and modulatory functions that contribute to its critical integrative role in the central transmission of noxious stimuli. The thalamus receives axonal projections from spinal cord and brainstem neurons relaying innocuous (dorsal column pathway) and nociceptive (spinothalamic pathway) input from all peripheral receptors that are stimulated by spinal manipulation.

Identifying which (if any) of the clinician-controlled mechanical parameters of spinal manipulation can affect convergent ascending central processing could provide critical insight into the central mechanisms and clinical variables responsible for positive clinical outcomes of spinal manipulation. To begin to address this issue, a study was conducted to determine whether the single clinician-controlled mechanical parameter of high velocity low amplitude spinal manipulation (HVLA-SM) thrust duration alters mechanical trunk activation thresholds of adult rat nociceptive specific (NS) neurons in lateral thalamic nuclei.

Methods

Electrophysiology

All experiments were approved by Palmer's Institutional Animal Care and Use Committee. For electrophysiological recordings, 9 adult male Wistar rats (320 - 460g) were anesthetized with an intraperitoneal injection of 50% urethane (1.2g/kg) and maintained with supplement doses (5% urethane) administered intravenously as needed. The rat's head was secured in a stereotaxic device with its dorsal surface positioned horizontally. A small hole was made in the skull and the exposed dura was opened. The extracellular recording electrode was advanced into the thalamus.

Activity in lateral thalamic neurons was recorded extracellularly with DiI (1,1'-dioctabecyl-3,3,3',3'-tetramethyl-indocarbocyanine perchlorate)-coated tungsten microelectrodes (Fig. 1A) having 6 to 8 MΩ impedance. Thalamic electrode tracks were between -2.04 and -3.30mm caudal to bregma and 1.2 and 3.8mm lateral to midline. Recording began at 4mm below the surface of the cortex and ended at 7.5mm. Lateral thalamic nuclei through which the DiI-labeled electrode passed in each rat included: VL, VPL/VPM, Po, LDVL, LDDM. Neurons with cutaneous receptive fields on the dorsolateral trunk were characterized using graded mechanical stimuli (gentle stroking with a nylon brush and noxious pinch with a serrated forceps). Neurons failing to respond to innocuous stroking but responding to trunk pinch were classified as NS.

Mechanical Activation Threshold

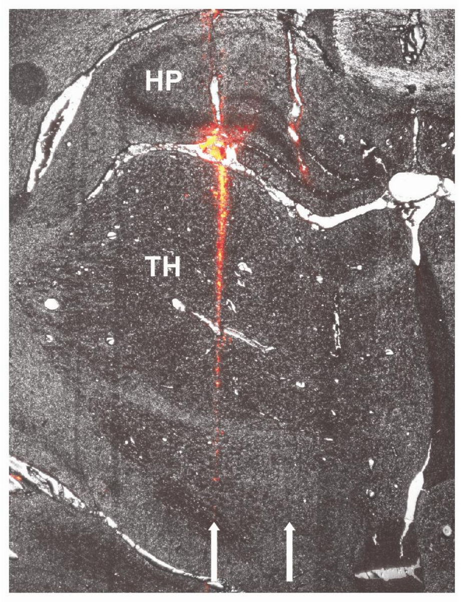
Once a thalamic neuron responsive to trunk stimulation was located, an electronic von Frey anesthesiometer (with a rigid tip adapter for deep pressure; 0.79mm^2 contact area) [IITC Model 2390; Fig. 1B) was used to apply mechanical stimuli (measured in grams) in each of three directions on the dorsum of the trunk: dorsal-ventral, 45˚caudalward and 45˚cranialward (Fig. 1C). It was thought that the direction in which a trunk stimulus was applied might differentially affect force transmission to the peripheral mechanoreceptors and thereby impact thalamic response thresholds. Electronic von Frey trunk stimuli were applied within 2 cm of the spine.

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 85% rat body weight over a duration of either 100 or 400ms. 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 on the intact skin overlying the L_5 spinous process. HVLA-SMs were separated by 5 minute intervals.

Figure 1

A.

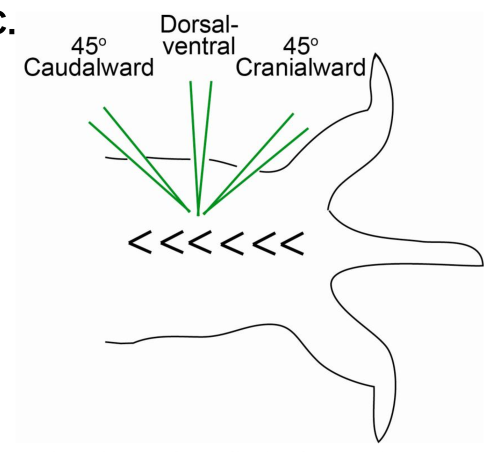


Example of lateral thalamic electrode tracks Hippocampus (HP), Thalamus (TH)

B.

Electronic von Frey IITC –Model 2390

C.



Directions of applied electronic von Frey trunk mechanical stimuli

Histology

Postmortem histological reconstructions of each DiI-labeled electrode track were made by taking measurements from mid-line at the appropriate thalamic anterior-posterior distance from bregma combined with carefully maintained records of electrode penetration depths from the cortical surface.

Results

Electrophysiological activity of 18 NS lateral thalamic neurons was recorded from 9 adult rats. All 18 NS neurons were found within two lateral thalamic nuclei [Po (n=6) and VL (n=12)] despite the inclusion of LDVL, LDDM, Po, VL, VPL, VPM nuclei within our search area (Fig. 2). There was no difference (P=.68) in the mean rate of spontaneous activity between the Po (8.22 imp/s; LCI 2.77; UCI 13.67) and VL (7.23 imp/s; 4.35,10.11) neurons. Therefore, results of the neurons from these two lateral thalamic nuclei were combined and analyzed together. Figure 3 shows an example of a VL NS neuron responding to mechanical trunk stimulation in the dorsal-ventral, 45˚ cranial, and 45˚ caudal directions using electronic von Frey anesthesiometer. Figure 4 shows the distribution of changes in mechanical trunk activation response thresholds for the 18 NS neurons to each of the three mechanical testing directions for each of the 3 HVLA-SM thrust durations.

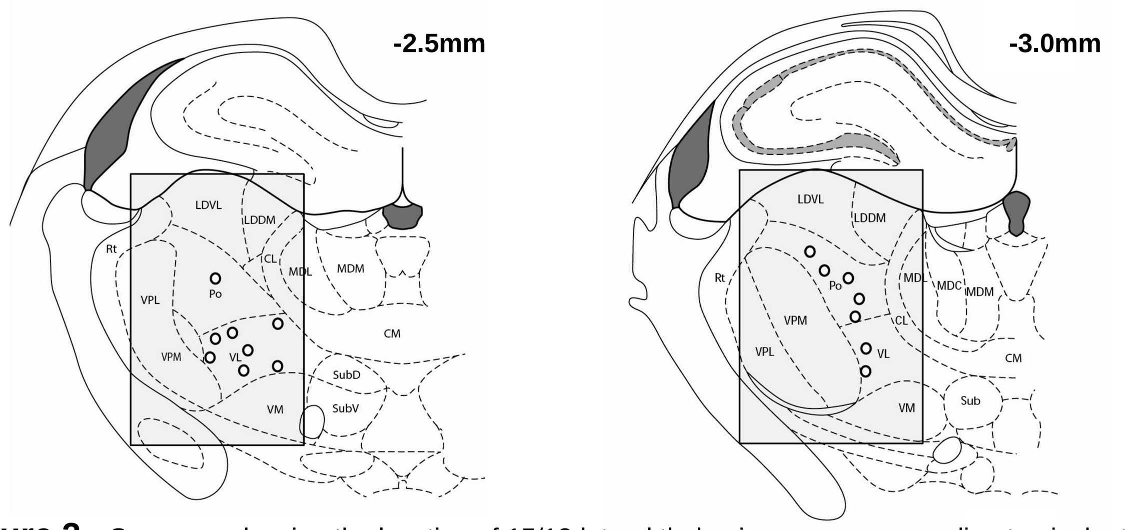


Figure 2. Summary showing the location of 15/18 lateral thalamic neurons responding to pinch stimuli applied to the trunk at -2.5mm and -3.0mm caudal to bregma (3/18 neurons located in adjacent sections).

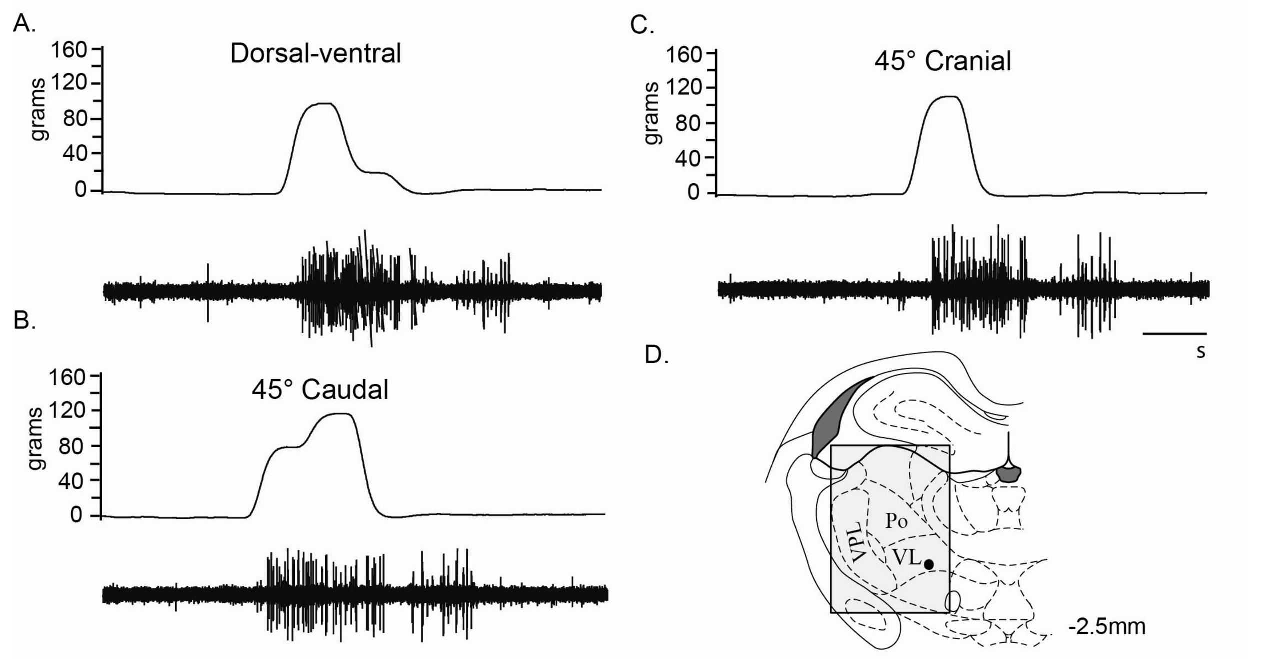


Figure 3. Raw electrophysiological recordings (lower row) of responses to lumbar trunk electronic von Frey stimuli (upper row) in the (A) dorsal-ventral (96.1 g), (B) 45˚ caudal (73.9 g) and (C) 45˚ cranial (106.7 g) directions. (D) The location of the trunk responsive VL neuron (●) was at the -2.5 mm caudal to bregma level.

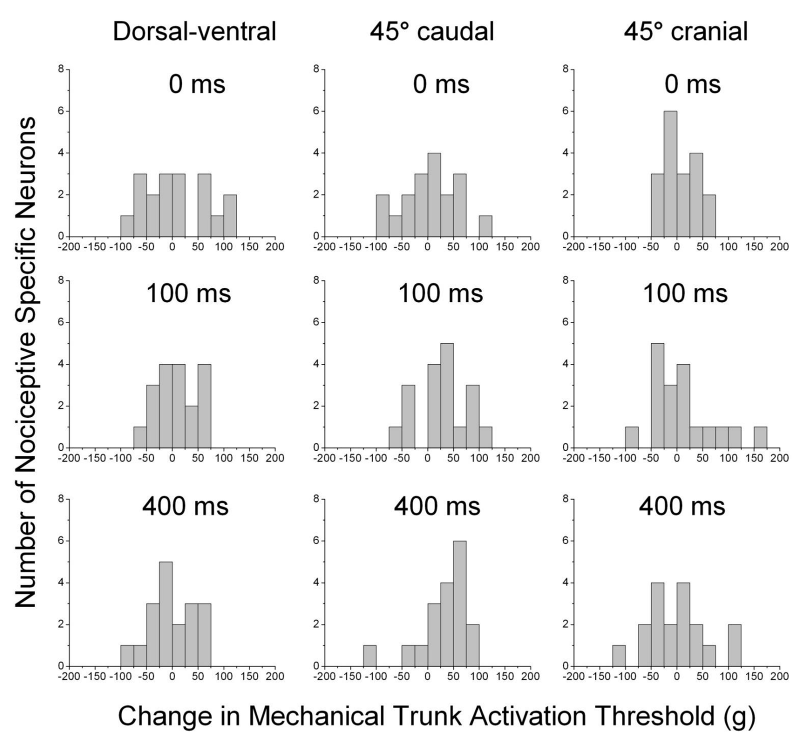


Figure 4. Frequency histograms of changes in trunk electronic von Frey mechanical activation response thresholds for the dorsal-ventral, 45˚ caudal and 45˚ cranial directions of NS lateral thalamic neurons following time-control (0ms), 100 and 400 ms HVLA-SM thrust durations.

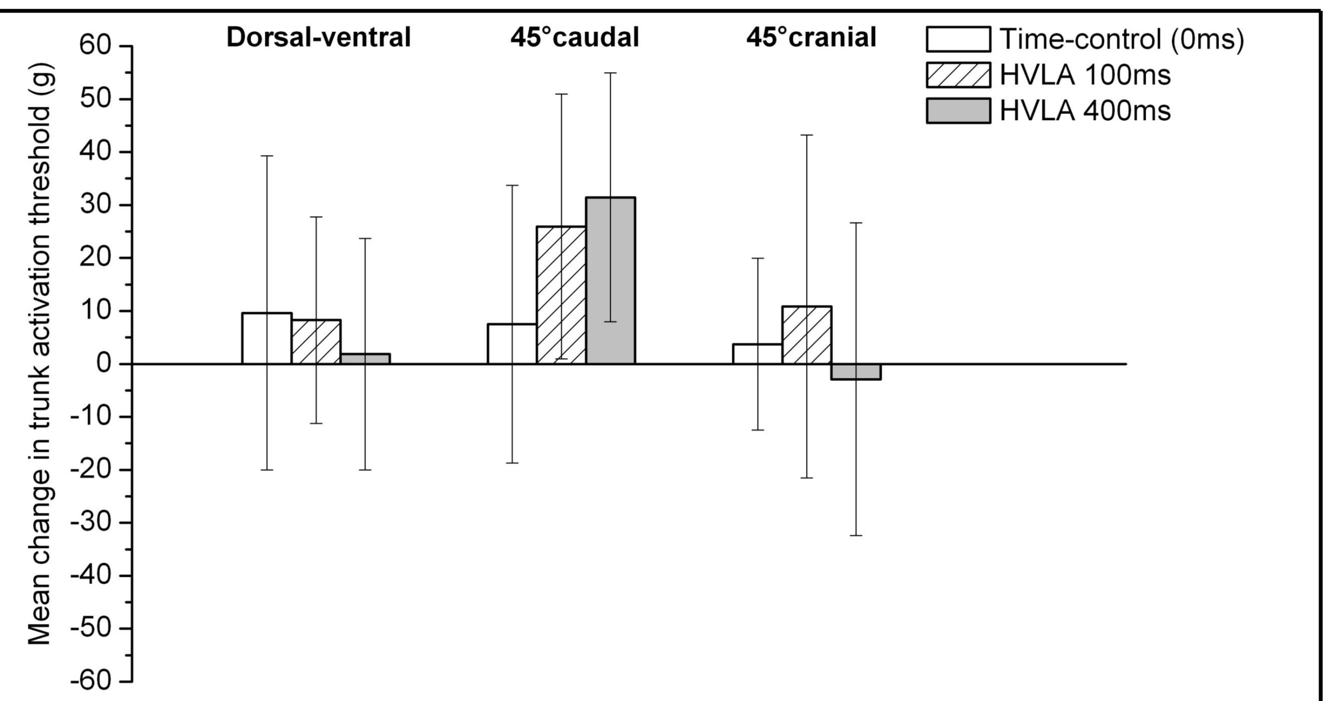


Figure 5. Mean change in lumbar trunk electronic von Frey mechanical activation response thresholds (grams) for the dorsal-ventral, 45˚ caudal and 45˚ cranial directions of NS lateral thalamic neurons following time-control, 100 and 400 ms HVLA-SM thrust duration. Data are reported as means and 95% confidence intervals (lower, upper 95% CI).

Data Analysis

Using a mixed model ANOVA analysis, mechanical activation thresholds for the NS lateral thalamic neurons were not significantly different between the time-control and 100 or 400ms HVLA-SM thrust durations for any of the 3 mechanical trunk stimuli directions tested (Fig. 5).

Conclusions

To our knowledge, this study is the first to investigate the effects of a clinician-controlled mechanical HVLA-SM parameter (thrust duration) on neural response properties of supraspinal neurons.

The data suggest that HVLA-SM duration does not alter mechanical activation thresholds of NS neurons in two lateral thalamic nuclei (VL, Po) when the dorsal trunk is mechanically stimulated in the dorsal-ventral, 45˚ caudal or 45˚ cranial directions.

The mean changes in mechanical activation threshold for the 100ms and 400ms thrust duration in the 45˚ caudal direction were greater in magnitude than the mean changes in the dorsal-ventral and 45˚ cranial directions.

Our use of a single application of the electronic von Frey mechanical stimulus to the trunk in a given direction before and after a spinal manipulation may have contributed to the variability we observed in thalamic responses (Fig.5).

Due to the thalamus' critical importance in nociceptive somatosensory processing, larger studies that include these and other lateral (VPL ,VPM) and medial (Sm, MD,CM) thalamic nuclei known to be involved in pain processing should be performed in normal, acute, and chronic pain animal models. In addition, the effects of HVLA-SM parameters on other types of neurons such as wide dynamic range neurons should also be investigated.

Thalamic Nuclei Abbreviations: central medial (CM), laterodorsal dorsomedial(LDDM), laterodorsal ventrolateral (LDVL), mediodorsal (MD), submedius (Sm) , posterior (Po), ventrolateral (VL), ventral posterolateral (VPL), ventral posteromedial (VPM).

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