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Effects of Thrust Magnitude and Duration on Immediate Post-Spinal Manipulation Trunk Muscle Spindle Responses

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Abstract

Objective: The purpose of this study was to characterize trunk muscle spindle responses immediately after high velocity, low amplitude spinal manipulation (HVLA-SM) delivered at various thrust magnitudes and thrust durations.

Methods: Secondary analysis from multiple studies involving anesthetized adult cats (n = 70; 2.3–6.0 kg) receiving L6 HVLA-SM. Muscle spindle afferent recordings were obtained from L6 dorsal rootlets prior to, during, and immediately after HVLA-SM. L6 HVLA-SM was delivered posterior-to-anterior using a feedback motor with peak thrust magnitudes of 25, 55, 85% of cat body weight (BW) and thrust durations of 25, 50, 75, 100, 150, 200, and 250ms. Time to 1st action potential (AP) and muscle spindle discharge frequency during 1 and 2s post-HVLA-SM were determined.

Results: A significant association between HVLA-SM thrust magnitude and immediate (≤ 2s) muscle spindle response was found ($p < 0.001$). For non-control thrust magnitude pairwise comparisons (25%, 55%, 85%BW), 55%BW thrust magnitude had the most consistent impact on immediate post-HVLA-SM discharge outcomes (FDR < 0.05). No significant association was found between thrust duration and immediate post-HVLA-SM muscle spindle response ($p > 0.05$).

Conclusion: We found that HVLA-SM thrust magnitudes delivered at 55%BW were more likely to impact immediate (≤ 2s) post-HVLA-SM muscle spindle response.

MeSH

Muscle Spindles; Manipulation Spinal; Musculoskeletal Manipulations; Neurophysiology; Back Muscles

INTRODUCTION

Low back pain (LBP) is considered the global leading cause of years lived with disability affecting over 500 million individuals.(1) Despite LBP's large socioeconomic implications, pharmacological management of chronic LBP has had limited success and most often relies on opioid-related pharmacy which has become increasingly associated with drug misuse/abuse.(2–4) Thus, there remains an urgent need for more clinically effective non-pharmacological therapeutic interventions that can minimize LBP severity, episode duration, and/or help prevent the transition from acute to chronic LBP.

High velocity low amplitude spinal manipulation (HVLA-SM) is a non-pharmacological therapeutic approach commonly used by chiropractors, physical therapists, and osteopaths to treat acute and chronic LBP.(5–8) Evidence-based guidelines currently recommend the use of conservative approaches (such as HVLA-SM) as initial treatments for non-specific LBP.(9–13) Establishment of validated clinical prediction rules to help identify those individuals most likely to experience positive outcomes with HVLA-SM would be beneficial; however

for such to occur, elucidation of the underlying neurophysiological mechanisms involved will most likely be required. Mechanistic-oriented investigations will assuredly entail a greater use of animal models due to the related invasive procedures often required.

While there is no consensus regarding the neurophysiological mechanisms responsible for HVLA-SM clinical efficacy, several theories involving neuromuscular response have been espoused.(14–16) For example, spinal mechanoreceptor stimulation and the resulting afferent barrage caused by HVLA-SM delivery has been proposed to inhibit spinal reflex responses via a muscle spindle pathway.(14, 17–19) Intrafusal fibers of the muscle spindle receptor are innervated by γ-motor neurons which in turn govern the sensitivity (or gain) of the spindle response to subsequent changes in muscle length.(20) Johansson and Sojka proposed and experimentally tested a nociceptive-proprioceptive hypothesis in which pain-induced hyperactivation of group III and IV nociceptive afferents would lead to changes γ-motor neuron sensitivity and thereby alter muscle spindle responsiveness to muscle stretch, yielding hyperexcitability of α-motor neurons and subsequent hypertonicity in affected muscles.(21) Despite strong experimental evidence supporting the Johansson and Sojka's hypothesis,(22–28) experimental(29, 30) and clinical(31–33) evidence refute the existence of such a nociceptive-proprioceptive relationship. Additional work is required to bring greater clarity regarding how HVLA-SM and musculoskeletal pain both impact muscle spindle responsiveness to stretch, γ-motor, and/or α-motor activity.

The relationship between trunk muscle spindle responses evoked by the physical characteristics of HVLA-SM delivery (i.e. thrust magnitude, thrust duration, thrust direction, anatomical location, and the impact of soft tissue preload) has been extensively investigated over the last decade using a feline model.(34–45) Collectively, these studies indicate that: (a) higher frequency muscle spindle discharge elicited during HVLA-SM thrust delivery begins to occur around the clinically relevant thrust duration of ≤ 150ms and that muscle spindle discharge rate tends to plateau as the thrust rate is increased to > 300N/s and/or thrust velocities > 20–30mm/s;(44) (b) a smaller preload magnitude (18% vs 43%) and a longer preload duration (4s vs 1s) increase mean spindle response during HVLA-SM thrust delivery; (34) (c) HVLA-SM delivered at any of 3 distinct L6 vertebral contact sites (spinous process, lamina, inferior articular process) similarly increase spindle discharge during HVLA-SM thrust delivery with no significant differences in spindle discharge occurring between the different L6 sites. Additionally, lower levels of spindle discharge are observed during thrust delivery at L7 when compared to L6 (when recording spindle afferent activity from the L6 dorsal root);(37) and (d) HVLA-SM delivered at different thrust directions similarly increase spindle discharge during HVLA-SM thrust delivery independently of the direction the thrust is being delivered.(45) All the aforementioned studies focused on changes in muscle spindle discharge during the delivery of the HVLA-SM thrust itself (from thrust onset to peak force), while less attention was directed toward post-HVLA-SM recovery of muscle spindle discharge after the HVLA-SM peak force had been delivered. Focus on spindle response during the HVLA-SM thrust phase can be attributed to the long-held importance placed on the HVLA-SM delivery velocity, as well as the observation that muscle spindle discharge typically returns to baseline discharge frequency relatively quickly after passive muscle stretch.

The purpose of this secondary analysis was to characterize the immediate (≤ 2s) post-HVLA-SM trunk muscle spindle response following a range of HVLA-SM thrust magnitudes and thrust durations. While multiple mechanisms influence muscle spindle recovery following passive stretch,(46–48) based primarily on the intrafusal fiber slack known to occur at the end of each muscle fiber shortening phase, we hypothesized that: (a) shorter thrust durations will decrease post-HVLA-SM's time to 1st action potential (AP; milliseconds) and increase spindle discharge frequency (Hz) during 1 and 2s periods post-HVLA-SM, and (b) greater thrust magnitudes will increase post-HVLA-SM time to 1st AP, and decrease spindle discharge during 1 and 2s post-HVLA-SM.

Materials and Methods

This work involves secondary analysis from data collected from multiple studies spanning nearly a decade involving a feline experimental preparation where similar modes of HVLA-SM delivery were used. All experiments were approved by the Institutional Animal Care and Use Committee of Palmer College of Chiropractic. Trunk muscle spindle discharge was recorded prior to, during, and following delivery of a simulated L6 HVLA-SM in deeply anesthetized male and female adult cats (n = 70, 2.3–6.0 kg, 709 individual recordings). General surgical procedures have been described in greater detail elsewhere.(35, 44, 49–52) Briefly, anesthesia was induced by isoflurane. Blood pressure as well as anesthesia levels (Nembutal 35 mg/kg, iv; Oak Pharmaceuticals, Lake Forest, IL) were monitored and maintained by catheters placed in the carotid artery and external jugular vein. Animals were mechanically ventilated and arterial pH, PCO_2, and PO_2 were maintained within the normal range (pH 7.32–7.43; PCO_2, 32–37 mmHg; PO_2, >85 mmHg) throughout the experiment. A laminectomy at the L5 level was performed exposing L6 dorsal rootlets which were teased and placed onto a monopolar electrode to obtain single unit afferent activity. All afferents were identified as muscle spindles by their increased discharge to succinylcholine (100 mg/kg; Butler Schein, OH), sustained response to a fast vibratory stimulus (~70 Hz), and/or decreased discharge to muscle twitch caused by bipolar direct muscle stimulation (0.2–0.3 mA; 50 μs).(35, 40, 50, 53)

Ethics approval and consent to participate

The experimental protocols for animal usage were reviewed and approved by Institutional Animal Care and Use Committee of Palmer College of Chiropractic following the National Institutes of Health guide for the care and use of laboratory animals (NIH Publications No. 96–01) revised in 1996.

Simulated HVLA Spinal Manipulation

All simulated HVLA-SM thrusts were delivered in a vertical (posterior-to-anterior) direction using a dual mode lever system with a force range from 0 to 50N (Aurora Scientific, Lever System Model 310). Rotation of the motor's shaft was computer-controlled and a lever arm was attached to the motor's shaft. Attached to the lever arm was a custom built rotary-to-linear converter, which in turn held a plexiglass manipulandum (for a more detailed description of the HVLA-SM manipulation device and associated manipulation protocols, please see (44, 45)). HVLA-SMs were delivered under force control either directly onto

the exposed L6 spinous process or through the intact cutaneous tissue overlying the L6 spinous process. Thrust magnitudes were applied at 0 (non-thrust control), 25, 55, 85% of the individual or averaged cat body weight (BW, 3.95 kg).(40, 44) Thrust durations used included 0 (non-thrust control), 25, 50, 75, 100, 150, and 250ms. The delivery order for individual combinations of thrust magnitudes and thrust durations were randomized with a 5-minute rest interval between thrusts to allow adequate time for recovery of viscoelastic properties of paraspinal soft tissues.(40)

Statistical Analysis

Muscle spindle discharge was recorded prior to, during, and 2 seconds post HVLA-SM delivery. Frequency of spindle discharge was determined using the number of action potentials occurring during the specific post-HVLA-SM time interval (1 or 2s). The post-HVLA-SM time period began at peak HVLA-SM thrust force or by a keyboard initiated data marker for non-thrust control protocols. All data were presented as mean ± SD (Table 1) and the normality assumption was evaluated using Q-Q plots. A two-way analysis of variance (ANOVA) was conducted first to examine the effects of thrust magnitude and thrust duration on each of the outcomes including post-HVLA-SM time to 1st AP (milliseconds) and spindle discharge frequency (Hz) during 1s and 2s post-HVLA-SM. Given a significant ANOVA, the post hoc comparisons between groups of interest were conducted with a two sample t test. Given the large number of comparisons, the false discovery rate (FDR) was used to correct for multiple comparisons.(54, 55) Instead of p-value, an FDR < 0.05 was used to reject the null hypothesis and considered to be statistically significant. All the analysis was conducted using SAS 9.4 (Cary, NC).

Results

Data were normally distributed and descriptive statistical results (Mean ± SD) for all three outcomes are shown in Table 1.

Thrust Magnitude and Immediate Post-HVLA-SM Muscle Spindle Response

A significant association was found between thrust magnitude and the immediate muscle spindle responses post-HVLA-SM (Table 2; post-HVLA-SM time to 1st AP [$p < 0.0001$]; spindle discharge frequency during 1s [$p < 0.0001$]; and during 2s [$p = 0.0002$]). Post-hoc comparisons between the different thrust magnitudes followed by FDR corrections showed that compared to control (0ms/non-thrust), 55%BW HVLA-SM created significant post-HVLA-SM changes in all 3 outcome measures at every thrust duration (FDR < 0.05; Table 2). For 55%BW HVLA-SM, the time to 1st AP increased and spindle discharge decreased during both 1 and 2s post-HVLA-SM.

For all non-control comparisons between different thrust magnitudes, significantly longer times to 1st AP were observed for 55% vs 25%BW at 50ms and at 250ms thrust durations (FDR=0.003 and FDR=0.033, respectively; Table 2). In addition, comparisons between 55% vs 85%BW at 50ms thrust duration was significant (FDR=0.027; Table 2). Significant decreases in discharge frequency during 1 second post-thrust were found for 55% vs 25%BW at both the 25 and 50ms thrust duration (FDR=0.047 and FDR=0.025, respectively;

Table 2); as well as between 85% vs 55%BW at 50ms thrust duration (FDR=0.04; Table 2). Moreover, a significant decrease in discharge frequency during 2 seconds post-HVLA-SM thrust was found for 55% vs 85%BW at 50ms thrust duration (FDR=0.047; Table 2). For all other non-control HVLA-SM between group thrust magnitude comparisons, no significant differences were found (FDR > 0.05, Table 2).

Thrust Duration and Immediate Post-HVLA-SM Muscle Spindle Response

No significant association was found between thrust duration and immediate post-HVLA-SM muscle spindle responses ($p > 0.05$).

Discussion

Changes in muscle spindle responsiveness related to alterations in muscle spindle gain or sensitivity to stretch is thought to be an important contributor to the overall physiological responses associated with HVLA-SM and/or possibly to its clinical benefits.(14, 17, 56) In the current study, we conducted a secondary analysis of data collected from multiple studies conducted over nearly a decade involving HVLA-SM in a feline preparation with the primary purpose of determining the relationship between both HVLA-SM thrust magnitude and duration and the immediate (≤ 2s) post-HVLA-SM paraspinal muscle spindle responses. While a main effect of HVLA-SM thrust duration (defined as thrust onset to peak force) on immediate (≤ 2s) post-HVLA-SM's spindle response was not found, thrust magnitude significantly altered spindle response immediately (≤ 2s) following the delivery of HVLA-SM. Overall, this study found that HVLA-SM thrust magnitudes delivered at 55%BW were more likely to alter immediate (≤ 2s) post-HVLA-SM spindle response compared to other thrust magnitudes. To our knowledge, this is the first time that immediate (≤ 2s) post-HVLA-SM muscle spindle response has been analyzed, particularly in such a large sample size.

HVLA-SM thrusts delivered at 55%BW increased the incidence of significant changes in the immediate (≤ 2s) post-HVLA-SM spindle responses when compared to 25% and 85%BW (Table 2). These results did not support our initial hypothesis that greater thrust magnitudes (i.e. 85%BW) would elicit increased time to first AP and/or decreased spindle discharge frequency during 1 and 2s post-HVLA-SM. However, these findings do suggest that a complex interaction exists between HVLA-SM thrust magnitude and immediate post-HVLA-SM spindle response. Understanding the clinical and neurophysiological importance of HVLA-SM magnitude on post-HVLA-SM will require additional investigation, as at this time it is currently unknown whether this relationship impacts HVLA-SM clinical efficacy. In a recent study using a feline preparation and a commercially available Activator IV® HVLA-SM device delivering thrust magnitudes of approximately 35N, 63N, and 102N (as derived from spinal tissue analog testing), we reported that the mean time to first AP was 54, 465, and 607ms respectively. (38) Likewise using a different HVLA-SM commercial device (Pulstar®), the mean time to the first AP was 229, 289, and 284ms for three increasing thrust magnitudes (22N, 44N, 67N). (38) These initial findings using commercial HVLA-SM devices support the concept that thrust magnitude impacts time to the 1st AP post-HVLA-SM in a somewhat linear fashion. However, these commercial devices also deliver HVLA-

SM thrusts at much shorter thrust durations (2–3ms) compared to thrust durations in the present study (25–250ms). Differences in HVLA-SM thrust force generation and/or shorter thrust delivery durations may be responsible for these post-HVLA-SM differences.

Our previous work demonstrated that shorter HVLA-SM thrust durations (≤ 150ms) compared to longer thrusts durations significantly increase spindle discharge during the delivery of the HVLA-SM thrust itself.(44, 57) However, these previous studies failed to evaluate HVLA-SM effect on post-HVLA-SM spindle discharge recovery. This current study indicates that there was no relationship between thrust duration and spindle afferent response immediately (≤ 2s) after HVLM-SM thrust delivery. Thus, these findings failed to support our initial hypothesis that shorter HVLA-SM thrust durations would significantly impact all three immediate post-HVLA-SM outcomes regardless of thrust magnitude. Anatomical and/or physiological limitations naturally inherit to muscle spindle apparatus may be a limiting factor to the resumption of resting spindle discharge following short HVLA-SM thrust durations. The brevity of the HVLA-SM mechanical stimulus is somewhat unique and rarely encountered in natural settings and/or tested experimentally. The neurophysiological effects of such short duration passive muscle stretch on spindle discharge recovery has not been investigated nearly to the extent of much slower delivered ramp and hold muscle stretch, leaving much to be learned physiologically related to these unique types of mechanical stimuli.

While clinical consequences of muscle spindle activity evoked during and/or after HVLA-SM delivery cannot be determined directly from animal studies, animal studies do provide essential physiological information related to our understanding of the neurophysiological consequences of HVLA-SM. Animal studies become particularly important since microneurography in humans is limited to superficial peripheral nerves which are accessible to needle insertion through the skin (i.e. radial, tibial, common peroneal).(58) These microneurography limitations put proximal and axial muscle spindle recordings in humans beyond current experimental reach.(58) Animal studies involving HVLA-SM have also brought much needed attention to the urgent need for clinical research studies to begin capturing biomechanical data related to HVLA-SM delivery, so as to better determine the relationships between HVLA-SM biomechanical delivery characteristics, neurophysiological responses, and clinical outcomes.(59)

Limitations

Limitations associated with this study include: (1) HVLA-SM was delivered using either forceps directly attached to the L6 spinous process or a plexiglass manipuland tip applied to cutaneous tissue directly overlying the L6 spinous process. When the manipuland tip was used, soft tissues overlying the L6 spinous process were slightly compressed (preloaded) prior to delivery of the HVLA-SM. This was intended to minimize differences in L6 vertebral movement during the HVLA-SM caused by the two types of contact. Regardless of HVLA-SM delivery method, all trunk muscle spindle receptive fields were caudal and/or lateral to the L6 spinous process, and simulated spinal manipulation was directed in a posterior-to-anterior direction only. A manually delivered HVLA-SM is typically directed with inferior-superior or medial-lateral components depending upon the plane line of either

the facet joints or intervertebral disc This specific aspect of HVLA-SM delivery was not taken into account in the present study; (3) HVLA-SM was not being delivered at the end-range of the vertebral motion. Clinically, spinal manipulative thrusts are often delivered at or near the end of the vertebral range of motion in order to distract, gap and in some instances cavitate the spinal facet joints. We did not bring L6 to its end range of motion in the attempt to minimize possible nerve fiber damage/tearing from the recording electrode; and (4) physiological differences do exist between feline and human species as it pertains to spinal joint mobility. For instance, previous studies have shown that joint stiffness, both at segmental level and at the lumbar region as a whole, tends to be greater (up to 7x) in humans compared to felines. (60) This decrease in joint stiffness in the feline spine has been associated with greater vertebral translation, intervertebral motion, and/or joint strain during HVLA-SM delivery.(61) Knowing such information, it was also concluded that the feline can indeed be used as an appropriate model for investigating local versus regional physiological affects during HVLA-SM.(61–63)

Future Studies

Unlike studies performed by Johansson and colleagues,(23, 24, 64) it should be noted that all studies involved in this secondary analysis, as well as those looking at post-HVLA-SM effects following extremely short HVLA-SM thrust durations (2–5ms) using commercial HVLA-SM devices,(36, 38) were performed in preparations with non-inflammatory or non-chemosensitized tissue environments. To provide greater understanding of the immediate and longer-term post-HVLA-SM effects on muscle spindle responses, HVLA-SM needs to be delivered in inflammatory or chemosensitized tissue environments, such as that which occurs during acute and/or chronic LBP.

Conclusions

We demonstrated that overall thrust magnitudes delivered at 55%BW are more likely to change post-HVLA-SM immediate (≤ 2s) muscle spindle response when compared to other HVLA-SM thrust magnitudes. Shorter thrust durations and higher magnitude thrusts did not uniformly increase immediate post-HVLA-SM response, suggesting that specific HVLA-SM delivery characteristics may be more desirable than others to impact immediate post-HVLA-SM spindle response. Future investigations should determine the neurophysiological impact of extremely short HVLV-SM thrust durations (2–5ms) at various HVLA-SM thrust magnitudes on immediate post-HVLA-SM muscle spindle response and recovery. In addition, similar post-HVLA-SM spindle response studies should be performed in experimental preparations having reduced joint mobility and/or inflammatory/chemosensitized environments. Further characterization of the neurophysiological effects of HVLA-SM is imperative to provide a more complete picture of the biological impact of HVLA-SM, as this new knowledge will be used to eventually identify the underlying physiological mechanisms responsible for the clinical efficacy of HVLA-SM.

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Joel Pickar-provided comments on the manuscript, some of the data analyzed came from a project funded by NIH prior to his retirement.

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Practical Applications of your study

Biomechanical characteristics of HVLA-SM thrust alter immediate post-HVLA-SM trunk muscle spindle recovery response.

HVLA thrust magnitude of 55% body weight (BW) was more effective than 25% or 85%BW at impacting immediate (≤ 2s) post-HVLA-SM trunk muscle spindle response, particularly at shorter thrust durations (≤ 50ms).

There was no relationship between HVLA-SM thrust durations (25, 50, 75, 100, 150, 250ms) and immediate (≤ 2s) post-HVLA-SM trunk muscle spindle response.

Greater investigation of post-HVLA-SM impact on recovery response of muscle spindle discharge will be required to determine whether this neurophysiological effect of HVLA-SM contributes to clinical outcomes.

Table 1.

Descriptive Statistics of Mean Values

%BW	Duration (ms)	Outcome	N	M (ms)	SD	Outcome	N	M (Hz)	SD	Outcome	N	M (Hz)	SD
0	0	Time to 1st AP (ms)	118	36	0.026	1s post-thrust (Hz)	118	31.58	10.48	2s post-thrust (Hz)	118	31.43	10.89
25	25		27	76	0.030		27	26.37	9.72		27	27.93	9.61
	50		30	100	0.148		30	25.60	11.82		30	28.41	11.00
	75		30	99	0.116		30	25.80	10.93		30	27.53	10.90
	100		30	104	0.119		30	23.70	9.75		30	25.60	9.41
	150		32	113	0.128		32	25.28	11.67		32	27.23	12.21
	250		28	95	0.058		28	25.07	10.03		28	27.98	10.01
55	25		19	176	0.206		19	19.00	7.30		19	21.84	6.48
	50		19	260	0.269		19	17.11	8.66		19	20.03	8.18
	75		75	176	0.263		75	22.29	10.62		75	25.01	10.55
	100		56	147	0.149		56	22.30	10.08		56	25.15	9.49
	150		56	171	0.195		56	21.66	10.49		56	24.35	10.09
	250		60	187	0.236		60	20.70	11.06		60	23.88	10.13
85	25		22	107	0.058		22	25.32	12.78		22	26.34	13.76
	50		22	127	0.086		22	25.18	13.20		22	27.25	13.28
	75		22	125	0.082		22	25.77	12.22		22	27.48	12.98
	100		23	127	0.097		23	26.17	12.95		23	28.76	12.52
	150		19	131	0.088		19	25.11	14.02		19	27.50	13.85
	250		21	136	0.082		21	24.43	13.24		21	27.35	13.56

Note: %BW= % of body weight; ms=milliseconds; AP= action potential Hz= Hertz; N= sample; M= mean; SD= standard deviation.

Table 2.

FDR for Thrust Magnitude vs Immediate Post-HVLA-SM Muscle Spindle Response

Duration (ms)	Comparisons among %BW	Time to 1st AP	1s post-thrust	2s post-thrust	Duration (ms)	Time to 1st AP	1s post-thrust	2s post-thrust	Duration (ms)	Time to 1st AP	1s post-thrust	2s post-thrust
25ms	0% vs. 25%	0.295	0.048	0.263	50ms	0.082	**0.025**	0.296	75ms	0.082	**0.028**	0.237
	0% vs. 55%	**0.002**	**<.0001**	**0.004**		**<.0001**	**<.0001**	**0.0002**		**<.0001**	**<.0001**	**0.0009**
	0% vs 85%	0.082	**0.034**	0.170		**0.033**	**0.032**	0.247		**0.033**	**0.046**	0.263
	25% vs. 55%	0.062	**0.048**	0.187		**0.003**	**0.025**	**0.046**		0.052	0.201	0.366
	25% vs. 85%	0.555	0.831	0.711		0.602	0.945	0.793		0.602	0.993	0.985
	55% vs 85%	0.236	0.109	0.296		**0.027**	**0.040**	0.137		0.261	0.246	0.419
Duration (ms)	**Comparisons among %BW**	**Time to 1st AP**	**1s post-thrust**	**2s post-thrust**	**Duration (ms)**	**Time to 1st AP**	**1s post-thrust**	**2s post-thrust**	**Duration (ms)**	**Time to 1st AP**	**1s post-thrust**	**2s post-thrust**
100ms	0% vs. 25%	0.062	**0.003**	**0.046**	150ms	**0.033**	**0.019**	0.187	250ms	0.117	**0.020**	0.263
	0% vs. 55%	**<.0001**	**<.0001**	**0.0036**		**<.0001**	**<.0001**	**0.0009**		**<.0001**	**<.0001**	**0.0002**
	0% vs 85%	**0.033**	0.053	0.366		**0.033**	**0.039**	0.269		**0.027**	**0.022**	0.263
	25% vs. 55%	0.295	0.666	0.906		0.140	0.201	0.342		**0.033**	0.128	0.247
	25% vs. 85%	0.628	0.499	0.366		0.688	0.983	0.958		0.432	0.915	0.906
	55% vs 85%	0.628	0.214	0.296		0.405	0.295	0.366		0.268	0.241	0.326

Note: FDR: false discovery rate; HVLA-SM: high velocity low amplitude spinal manipulation; ms: milliseconds; %BW: percentage of body weight; AP: action potential; 1s post thrust: discharge frequency during 1 second following thrust; 2s post thrust: discharge frequency during 2 seconds following thrust.