Motor Neuron Excitability Attenuation as a Sequel to Lumbosacral Manipulation in Subacute Low Back Pain Patients and Asymptomatic Adults: A Cross-Sectional H-Reflex Study

J. Donald Dishman, DC, MSc,[a] Jeanmarie R. Burke, PhD,[b] and Paul Dougherty, DC[b]

Abstract

Objective: The purpose of the study was to compare a time series of tibial nerve H-reflex trials between patients with subacute low back pain (LBP) and asymptomatic adults using pre and post high-velocity, low-amplitude (HVLA) spinal manipulation (SM) and control procedures.

Methods: Asymptomatic adults (n = 66) and patients with subacute LBP (n = 45) were randomized into 3 lumbosacral procedures: side-posture positioning, joint preloading with no thrust, and HVLA SM. A time series of 40 H_{max}/M_{max} ratios at a rate of 0.1 Hz were recorded in blocks of 10 trials at baseline and after the lumbosacral procedures at time points corresponding to immediately after, 5 minutes after, and 10 minutes after the procedure. Descriptive time series analysis techniques included time plots, outlier detection, and autocorrelation functions. A mixed analysis of variance model (group × procedure × time) was used to compare the effects of lumbosacral procedures on H_{max}/M_{max} ratios between the patients with subacute LBP and asymptomatic participants.

Results: The time series analysis and the significant lumbosacral × time interaction term ($P < .05$) indicated that inhibition of the H_{max}/M_{max} ratios at the 10-second postlumbosacral procedure time point was greatest after the HVLA SM procedure. The effects of lumbosacral procedures on H_{max}/M_{max} ratios were similar between patients with subacute LBP and asymptomatic participants.

Conclusions: Although nonspecific effects of movement or position artifacts on the H_{max}/M_{max} ratio were present, a reliable and valid attenuation of the H_{max}/M_{max} ratio occurred as a specific aspect of HVLA SM in both asymptomatic adults and patients with subacute LBP. (J Manipulative Physiol Ther 2018;41:363-371)

Key Indexing Terms: *Low Back Pain, Mechanical; Lumbar Manipulation; H-Reflex; Gastrocnemius Muscle*

Introduction

A time series of tibial nerve H-reflex trials or pre-post H/M recruitment curves has revealed an inhibition of the Ia afferent-alpha motoneuron pathway that was dependent upon the delivery of a high-velocity, low-amplitude (HVLA) spinal manipulation (SM) to the lumbosacral spine.[1,2] The effects of postural perturbations after various methods of lumbosacral spine manipulation, the stimulus-response segmental relationship between the lumbosacral spine and the gastrocnemius muscle (GM), and H-reflex methodological considerations have been rigorously addressed in previous research to document the validity and reliability of H-reflex responses after HVLA SM.[1,3-7] However, only one of these tibial nerve H-reflex studies conducted to date included a patient sample.[8] Although the report by Suter et al[8] dissents on the attenuation of H-reflex responses in asymptomatic participants after HVLA SM, attenuation of the H-reflex response after HVLA SM occurred in patients with nonspecific low back pain (LBP). Their side-posture testing position, the soleus as the test muscle, and sacroiliac joint manipulation are experimental design deviations that would need to be rigorously addressed to provide an explanation for this dissenting report. A factorial experimental design is necessary to compare various postural orientations, triceps surae muscle

[a] Clinical Neurosciences Institute, Palmer College of Chiropractic Florida, Port Orange, Florida.

[b] Research Department, New York Chiropractic College, Seneca Falls, New York.

Corresponding author: Jeanmarie R. Burke, PhD, Research Department, New York Chiropractic College, 2360 State Route 89, Seneca Falls, NY 13148. Tel.: +1 315 568 3869. (e-mail: *jburke@nycc.edu*).

Paper submitted June 15, 2017; in revised form October 26, 2017; accepted October 26, 2017.

0161-4754

https://doi.org/10.1016/j.jmpt.2017.10.015

recording sites for H-reflex measurements, and methods of lumbosacral SM. As support for this recommendation, a previous study by Murphy et al[9] on sacroiliac joint manipulation using a prone H-reflex testing position reported an attenuation of the H-reflex response from the soleus muscle after the HVLA SM procedure in asymptomatic participants.

Inhibition of the Ia afferent-alpha motoneuron pathway as a unique stimulus-response to HVLA SM does not provide insights on the mechanisms that underlie the effectiveness of spinal manipulative therapy (SMT) in a clinical setting. However, surface electromyographic (EMG) recordings from the erector spinae muscles revealed that HVLA SM thrusts to lumbosacral spine evoked reflex responses in asymptomatic participants and patients with chronic LBP.[10,11] In addition to inhibition of the Ia afferent-alpha motoneuron pathway, other neurophysiological outcome measures (eg, facilitation of motor-evoked potentials after single-pulse transcranial magnetic stimulation,[12-14] increased V/M_{max} ratios,[2] modulation of motor-evoked potentials after paired-pulse transcranial magnetic stimulation,[15,16] and modulation of somatosensory-evoked potentials[17]) are evidence of unique stimulus-response effects of HVLA SM thrusts on neural pathways, including corticospinal, intracortical, and cerebellar. There are also unique stimulus-response patterns of afferent discharges to manipulative-like thrusts in animal models.[18-21] These data provide evidence that identifying a neurophysiological test as an indicator of "successful" delivery of an HVLA SM thrust may be promising as a translational tool for large-scale clinical research involving SM.[1,22]

The purpose of this study was to compare a time series of tibial nerve H-reflex trials between patients with subacute LBP and asymptomatic adults, pre-post HVLA SM, and control procedures. If results in patients with subacute LBP are similar to those in previous studies on asymptomatic adults, then the current study would provide further evidence that inhibition of the Ia afferent-alpha motoneuron pathway may be a neurophysiological indicator of a "successful" HVLA SM treatment.[1,2,8] The primary hypothesis was that inhibition of the Ia afferent-alpha motoneuron pathway would be greater after an HVLA SM thrust compared with SM control procedures of side-posture positioning and joint preloading with no thrust in both asymptomatic adults and patients with subacute LBP. The exploratory hypothesis was that the degree of inhibition of the Ia afferent-alpha motoneuron pathway after an HVLA SM thrust would be similar between asymptomatic adults and patients with subacute LBP. The rationale for the exploratory hypothesis was that an HVLA SM thrust evokes force, direction, and velocity-dependent afferent discharges from various mechanoreceptors that inhibit the Ia afferent-alpha motoneuron pathway regardless of the "resting" state of the lumbar musculoskeletal system (eg, hypertonicity of muscles or hypomobility of joints). From a therapeutic perspective, and beyond the scope of the current study, inhibition of the Ia afferent-alpha motoneuron pathway after an HVLA SM thrust may be a potential mechanistic response to reduce hypertonicity of lumbar muscles in subacute LBP patients—that is, reset the gain of the motoneuron pool to reduce hypertonicity.

Methods

Participants

A convenience sample of 66 healthy volunteers and 45 patients with subacute LBP participated in the study (Table 1). The healthy volunteers were first- and second-year chiropractic students who were recruited using campus advertisements and class announcements. Healthy volunteers who self-reported LBP within the past 12 weeks or had a history of spinal trauma, herniated nucleus pulposus, peripheral neuropathy, radiculopathy, or any other medical conditions were excluded from participation. Physical examination findings of neurologic abnormalities or hypertonicity of the lumbosacral musculature also excluded healthy volunteers from participation. The patients with acute LBP were referrals from a single private practice chiropractic office located in a suburb of Rochester, New York. The multidisciplinary practice included chiropractic practices, acupuncture, massage, exercise rehabilitation, and nutrition. The 2 referring chiropractors had over 20 years of clinical experience with a large patient volume.

Inclusion and Exclusion Criteria for Patients. Patients who were experiencing LBP that was confined to the lumbosacral region without any evidence of radicular pain into the lower extremities were identified as experiencing subacute LBP that was mechanical in origin. These patients met the inclusion criteria and were selected for this study. All patients fell into the category of subacute LBP, which was defined as a period of pain that did not exceed 12 weeks before enrollment in the study. All patients with subacute LBP who were referred to the study had previously undergone a routine series of plain-film radiographs to rule out fracture, dislocation, luxation, or osseous pathology. Upon neurologic screening by the clinician, there was no evidence of herniated lumbar intervertebral discs, cauda equina syndrome, canal stenosis, bowel or bladder dysfunction, peripheral neuropathy, or focal lumbosacral radiculopathy. In addition, a palpation examination performed by the clinician revealed exacerbation of pain upon deep palpation of the lumbar erector spinae musculature. Specifically, there was both a subjective response of increased pain by the patient and a palpation finding by the clinician of increased or hypertonic musculature. These palpation findings of taut and tender muscle fibers were consistent with pain-induced muscle spasm. During the patient history, any self-reported lumbar surgery or minimally invasive procedures, such as epidural steroid injections to treat LBP or metabolic disease that may lead to central or peripheral neurologic deficits including multiple

Table 1. *Characteristics of Patients (Mean ± SD)*

Group	L5-S1 Procedure	N	Sex (n)	Age (y)	Height (cm)	Weight (kg)	RMD (N = 24)	VAS (cm)	ODI (%)
Patients with subacute LBP	Spinal manipulation	15	10 M, 5 F	34.9 ± 8.88	173.9 ± 11.95	89.5 ± 23.67	7 ± 5.6	4 ± 2.2	24 ± 17.7
	Joint preloading	15	7 M, 8 F	37.8 ± 9.61	168.5 ± 8.68	83.8 ± 20.30	7 ± 4.5	5 ± 1.3	23 ± 9.8
	Side-posture positioning	15	6 M, 9 F	39.5 ± 12.57	170.9 ± 8.61	80.1 ± 12.84	7 ± 3.8	5 ± 1.9	24 ± 9.7
Healthy volunteers	Spinal manipulation	22	13 M, 9 F	25.6 ± 3.69	172.4 ± 8.74	73.5 ± 16.80			
	Joint preloading	22	14 M, 8 F	26.1 ± 5.42	171.6 ± 10.80	75.2 ± 12.81			
	Side-posture positioning	22	16 M, 6 F	24.5 ± 3.67	174.1 ± 11.88	78.2 ± 19.47			

F, female; *LBP,* low back pain; *M*, male; *ODI,* Oswestry Disability Index; *RMD,* Roland-Morris Disability Questionnaire; *SD,* standard deviation; *VAS,* visual analogue scale.

sclerosis or diabetes mellitus, excluded the patient with subacute LBP from participation. Ongoing or previous conservative spinal treatment including HVLA SM to treat LBP was not an exclusion criterion.

Disability and Pain Indices. After the informed consent process and before conducting the experimental protocol, all patients with acute LBP completed the Revised Oswestry Disability Index Questionnaire for LBP, the Roland-Morris Disability Questionnaire, and a 10-cm visual analogue scale to rate pain intensity at the time. The disability and pain indices provided a clinical description of the patients with subacute LBP enrolled in the study.

The local ethics committee reviewed and approved all experimental procedures in accordance with the criteria for the protection of human participants stated in the Common Rule (IRB Protocol Number: 99-06). All participants signed an informed consent form. The study was conducted from October 1999 to March 2004 with all data collection, data management, and primary statistical analysis being completed in this time frame.

Experimental Design

The factorial experimental design was group × lumbosacral procedure × time with repeated measures on the time factor. Using the procedures described by Cohen,[23] a sample size of 15 to 22 participants per lumbosacral procedure per group was deemed necessary to detect significant differences among the lumbosacral procedures from 10 to 60 seconds postprocedure and within each group with an alpha level of 0.05 and power of 0.80 and across large (f_{35}), medium (f_{25}), and small (f_{10}) effect sizes.

Lumbosacral Procedures

Details of the L5-S1 SM procedure, L5-S1 joint preloading procedure, and side-posture positioning were previously described.[1,7] The L5-S1 SM procedure consisted of a side-lying HVLA SM to the right side of the spine. The L5-S1 joint preloading procedure involved positioning the participant into side posture and applying manual contact to the joints of the right lumbosacral spine to increase tissue tension, but no thrust was applied. Side-posture positioning involved positioning the participant into side posture with manual contact to the paraspinal skin of the right L5-S1 zygapophyseal joints without tissue tension. The L5-S1 SM procedure with control procedures of L5-S1 joint preloading and side-posture positioning addressed the specific and nonspecific effects of an HVLA SM thrust on the Ia afferent-alpha motoneuron pathway within the factorial experimental design.

H-Reflex Methodology

As described in detail previously,[1] electrodiagnosis standards for evoking (Grass S88 Stimulator, Grass Instruments, West Warwick, Rhode Island) and recording M-wave and H-reflex EMG potentials (Grass P511 amplifier system, 10 Hz-1 kHz bandpass filter, Grass Instruments) from the medial head of the right GM were followed with the participant resting prone on a treatment table. The standard H/M recruitment curve was generated using a 1.0 ms square wave pulse from 0 to 150 V through a bipolar electrode configuration in the right popliteal fossa to determine the maximum M-wave response and the maximum H-reflex response from surface EMG recordings (10 mm Ag-AgCl electrodes).[24-27] When evoking the maximum H-reflex response, the submaximal M-wave response that also occurred was used to document the consistency of the stimulating and recording environments during the time series analysis.[25] After establishing the H_{max}/M_{max} ratio as the test reflex size, a time series of 10 H-reflexes were recorded, followed by the assigned lumbosacral procedure. Immediately after the lumbosacral procedure, and upon returning the participant to the prone testing position, another time series of 10 H-reflexes were recorded. Time series measurements of 10 H-reflexes were also repeated at 5 and 10 minutes after the lumbosacral procedures. The participants remained resting quietly in the prone testing position between time series measurements at the 5- and 10-minute postlumbosacral procedure time points. Time series measurements were recorded at a rate of 0.1 Hz to avoid the confounding influences of postactivation depression.[28] The maximum M-wave amplitude was recorded at the end of the test session to verify that impedance changes or electrode movement at the stimulating or recording sites did not occur.

Data Collection and Data Analysis

Computerized data acquisition and data analysis were performed using a 12-bit resolution analog-to-digital converter with a sampling rate of 5 kHz per channel, a digital output port to trigger the Grass S88 stimulator, and peak detection algorithms to mark the negative and positive peaks of the evoked EMG responses (LabVIEW, National Instruments Corporation, Austin, Texas). H-reflex recordings and delivery of the lumbosacral procedures for the healthy volunteers occurred within the Neuromuscular Research Laboratory at the chiropractic college, and these study procedures for patients with subacute LBP occurred in a treatment room within the referring chiropractic office. The electrophysiological instrumentation, computer data acquisition system, and adjusting tables were duplicated at both data collection sites. Each data collection site was assigned a licensed chiropractor with over 15 years of experience to deliver the lumbosacral procedures.

Statistical Analyses

Primary Statistical Analysis. A mixed analysis of variance model (group × lumbosacral procedure × time) with repeated measures on time was used to reveal the effects of a side-posture L5-S1 SM, side-posture joint preloading, and side-posture positioning in participants with and without subacute LBP on H_{max}/M_{max} ratios. The Dunnett's procedure for a priori contrast was used to detect any differences in H_{max}/M_{max} ratios between baseline values and postprocedure time points from simple, simple main effects of time within each group and lumbosacral procedure. All analyses were conducted using SPSS Version 13 for Windows (SPSS Inc, Chicago, Illinois). The level of significance was .05 for all statistical analyses.

Time Series Analysis. A time series analysis, as described previously, was performed on the data from the 66 healthy volunteers and 45 subacute LBP patients.[1] Each trial in the time series was normalized to the mean of the 40 trials in the time series and expressed as percent of the mean of H_{max}/M_{max} ratio with 100% being equivalent to the mean H_{max}/M_{max} ratio of the 40 trials in the time series. Event detection from the time series plots of the normalized data for each participant was defined as deviation from the mean of ±3 standard deviation (SD) units and confirmed by the Tukey's method of outlier detection: ($Q_1 - 3*IQR$, $Q_3 + 3*IQR$), where Q_1 is first quartile value, Q_3 is the third quartile value, and IQR is the interquartile range of the distribution.[1] Averaged time series plots for each lumbosacral procedure by group with event bars at ±1, ±2, ±3, and ±4 SD units were generated to compare the occurrences of unique events among lumbosacral procedures by group at each time point.

Autocorrelation coefficients were calculated across all participants within groups from 6 randomly generated data sets that were organized by participant number (1-37) and lumbosacral procedure (1-3) at each 10-second time point (± 100 seconds from baseline to immediately postprocedure). Control time points (±100 seconds) were randomly generated from time series at the 5- and 10-minute postlumbosacral procedure marks to be included in the autocorrelation analysis. Within this data management structure, autocorrelation coefficients predominately measured correlations between H_{max}/M_{max} ratios within lumbosacral procedures and control time points at lags ≤12 and between lumbosacral procedures and control time points at lags >12 for ±100 seconds.[1]

Intraclass correlation coefficients (ICCs) were used to assess the trial-to-trial variability of H_{max}/M_{max} ratios in the time series measurements before the lumbosacral procedures and at the 5- and 10-minute postlumbosacral procedure time points. Immediately postprocedure, the 10 H_{max}/M_{max} ratios represented not only the inherent trial-to-trial variability of H-reflex recordings, but also the time-varying postprocedural effects. Thus, calculating ICCs to determine the inherent trial-to-trial variability of H_{max}/M_{max} ratios immediately postprocedures would be negatively biased by time-varying postprocedural effects. To address the confounder of time-varying postprocedural effects, calculating the reliability (ICCs) of normalized H_{max}/M_{max} ratios at the 10-second postprocedure time point provided an index of the reliability of postprocedure effects, for example, reliability of inhibition of H_{max}/M_{max} ratios. Intraclass correlation coefficients of the normalized H_{max}/M_{max} ratios at the 10-second postprocedure time point were determined for 5 randomly generated data sets, which were created by randomly organizing the 37 participants per lumbosacral procedure into 12 repeated measurements of 3 trials. Intraclass correlation coefficients were also calculated after sorting the normalized H_{max}/M_{max} ratios at the 10-second postprocedure time point from high to low and again from low to high within each lumbosacral procedure. Control procedure data points were randomly generated from the first trials evoked at baseline and the 5- and 10-minute postlumbosacral procedure time points to be included in the ICC reliability analysis of immediate postprocedure effects. Standard errors of the measurements were also calculated as an index of reliability.

Results

Figure 1 summarizes the H_{max}/M_{max} ratios by group and lumbosacral procedure across time. Although H_{max}/M_{max} ratios decreased after all lumbosacral procedures, the decrease in the H_{max}/M_{max} ratio at 10 seconds postprocedure was significantly greater after HVLA SM compared

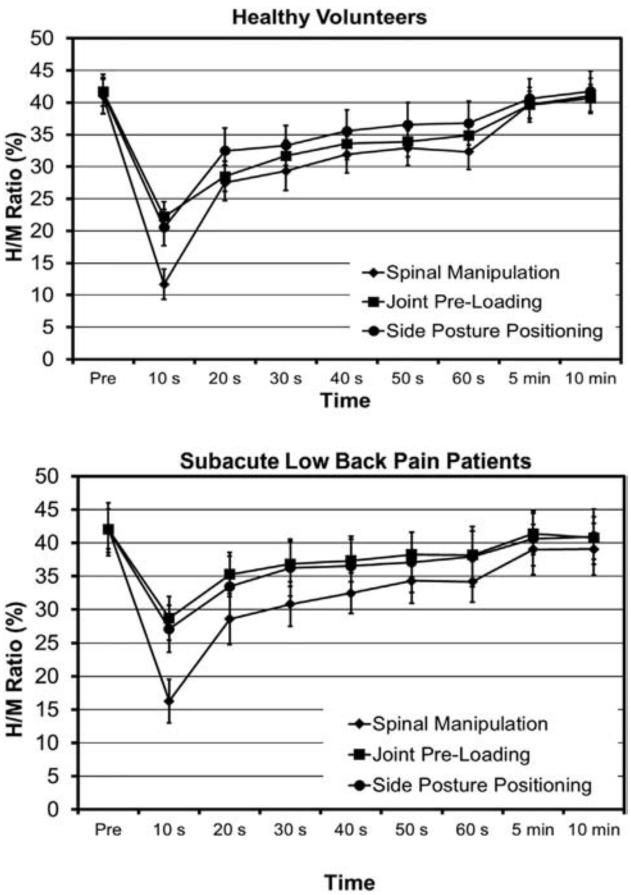

Fig 1. *Mean H_{max}/M_{max} ratios (± standard error) over time for healthy volunteers and subacute low back pain patients.*

with joint preloading and side-posture positioning and regardless of whether the participants were healthy volunteers or patients with subacute LBP ($P < .05$; $F[12\ 630]_{procedure \times time} = 4.66$). Lumbosacral procedure accounted for 15% of the variance in the H_{max}/M_{max} ratio at 10 seconds postprocedure ($\eta_p^2 = .15$). The simple, simple main effects of time within the lumbosacral SM procedure and group accounted for approximately 50% of variance in the H_{max}/M_{max} ratio for both the healthy volunteers ($\eta_p^2 = .48$) and patients with subacute LBP ($\eta_p^2 = .49$). Pearson correlation coefficients between the size of the H_{max}/M_{max} ratio at baseline and the amount of inhibition at the 10-second time point after the lumbosacral procedures were low ($r \le |.18|$); except for a moderate inverse correlation ($r = -.44$) among the patients with subacute LBP after HVLA SM; for example, the smaller the baseline H_{max}/M_{max} ratio, the greater the amount of inhibition.

The recovery to prebaseline H_{max}/M_{max} ratios was observed at 5 and 10 minutes after all lumbosacral procedures for both the healthy volunteers and the patients with subacute LBP. The ICCs for the 10 H_{max}/M_{max} ratios recorded at baseline and 5 and 10 minutes after lumbosacral procedures were ≥0.94, whereas standard errors of measurement were ≤3.2%.

The coefficient of variation at baseline and the 5- and 10-minute time points by group and lumbosacral procedure ranged from 4% to 8% (5.7% ± 3.78%). The maximum M-wave amplitudes and the amplitudes of the submaximum M-waves recorded on the H-reflex trials did not change throughout the test session.

Immediate postprocedures at the 10-second time point, event detection (>3 SD) occurred in approximately 70% of the participants receiving the lumbosacral SM procedure, while event detection occurred in ≤50% of participants in the joint preloading and side-posture positioning groups ($\chi^2_{df\ =\ 2} = 11.77, P < .05$) (Table 2). The Tukey method detected the same number of events as reported in Table 2. Any events (n = 11 of 3330 responses) detected during recordings at baseline and at the 5- and 10-minute postlumbosacral procedure time points indicated facilitation of the H_{max}/M_{max} ratio that was random among the participants. Additional inhibitory events (n = 41 of 999 responses) were detected during the immediate post-procedure trials, but these events corresponded to the recovery of the H_{max}/M_{max} ratio from the initial inhibitory event at the 10-second time point within a few participants (n = 21 of 111 participants).

Figure 2 shows the averaged time series plots by lumbosacral procedure for the healthy volunteers and subacute LBP patients. The normalized time series plots by participants within each lumbosacral procedure are not shown. Standard errors of measurement for the normalized 10 H_{max}/M_{max} ratios recorded at baseline and at the 5- and 10-minute postlumbosacral procedure time points were ≤5.6%. Postprocedure measurements at the 10-second time point, differences in normalized H_{max}/M_{max} ratios between lumbosacral SM, and joint preloading and side-posture positioning were greater than 5.6%. The lumbosacral SM procedure evoked an inhibition of the H_{max}/M_{max} ratio by 4 SDs from baseline responses, as compared to 2 to 3 SDs for the joint preloading and side-posture positioning procedures.

The ICC values for normalized H_{max}/M_{max} ratios at the 10-second time point were .61, .53, .53, .50, and .53 from the 5 randomly generated data sets and .98 when generating the data sets by ascending or descending order of the normalized responses. From the 6 randomly organized data sets, ranges of autocorrelation coefficients that were outside the “null” 95% confidence limits, $\pm 2/\sqrt{37}$ or ≥.32, only occurred at lags from 12 to 1 at 10 seconds postprocedure and time control: .44 to .57, .44 to .53, .34 to .51, .36 to .54, .32 to .53, and .37 to .60. Autocorrelation coefficients at all other time points and lags >12 were inside the “null” 95% confidence limits.

Discussion

The greater attenuation of H_{max}/M_{max} ratio, by approximately 10%, after HVLA SM, as compared with

Table 2. *Summary of the Time Series Event Detection Analyses at the 10-Second Time Point Immediately After the Lumbosacral Procedure (n [%])*

Group	Lumbosacral Procedure	No Event	Event Detected
Healthy volunteers	Spinal manipulation	7 (32)	15 (68)
	Joint preloading	14 (64)	8 (36)
	Side-posture positioning	11 (50)	11 (50)
Patients with subacute LBP	Spinal manipulation	4 (27)	11 (73)
	Joint preloading	11 (73)	4 (27)
	Side-posture positioning	11 (73)	4 (27)
Total	Spinal manipulation	11 (30)	26 (70)
	Joint preloading	25 (68)	12 (32)
	Side-posture positioning	22 (60)	15 (41)

LBP, low back pain.

side-posture positioning and joint preloading, was reliable and represented a physiological meaningful difference. Postprocedural effects had good reliability. Outlier detection algorithms and correlograms (eg, autocorrelation coefficients) revealed a pattern of non-randomness that was only time-locked to the lumbosacral procedures. Thus, the greater inhibition of the H_{max}/M_{max} ratios after HVLA SM, as compared with control lumbosacral procedures, was reliable because the post-procedural effects were reliable, nonrandom events. In agreement with the H-reflex literature and the standard error of measurement in the current study, physiologically meaningful differences for H_{max}/M_{max} ratios are 5% to 10%. However, the sensitivity and specificity of detecting inhibition of the normalized H_{max}/M_{max} ratio after the HVLA SM thrust as a unique event were only 70% and 64%, respectively.

The new insight provided by this research is that the unique stimulus-response characteristic of HVLA SM on the Ia afferent-alpha motoneuron pathway also occurred in patients with subacute LBP. The study sample of patients with subacute LBP met the criteria to be considered the most “appropriate” candidates for SMT. Patients with low back pain with the highest “appropriateness” ranking for SMT included those whose symptoms consisted of acute to subacute LBP, no gross neurologic deficits, no radiculopathy, no change in pain since onset, and no osseous pathology visible on plain-film radiography.[29] The patients with subacute LBP participating in the current study clearly met this well-accepted standard.

The patients with subacute LBP in the current study and the variety of pathologies affecting the lumbosacral region of symptomatic patients in the previous study by Suter et al[8] provide evidence that inhibition of the Ia afferent-alpha motoneuron pathway may be a neurophysiological indicator of a “successful” HVLA SM treatment. The use of H-reflex methodology as a translational tool for large-scale clinical research to measure the reliability of delivering the HVLA SM thrust would require gaining further insights on methodological considerations of triceps surae muscle recording sites and postural positions for recording the tibial nerve H-reflex responses. Other tibial nerve H-reflex studies may argue that measuring the area under the curve of the H/M recruitment curve, pre-post HVLA SM procedure, to document the inhibition of the Ia afferent-alpha motoneuron pathway would be a more robust neurophysiological indicator of a “successful” HVLA SM treatment.[2] Overall, either a time series of tibial nerve H-reflex trials or pre-post H/M recruitment curves reveal that inhibition of the Ia afferent-alpha motoneuron pathway is a unique stimulus-response characteristic of an HVLA SM procedure.[1-3,5-9,30-32] This unique stimulus-response characteristic of HVLA SM is also evident in patients with subacute LBP.

What remains problematic is that regardless of the H-reflex methodology, the neural biomarker of LBP and neuroplasticity that occurs as a sequel to SMT (clinical course of chiropractic care that results in alleviation of LBP and functional recovery) is still unknown. Reliable and valid changes in H-reflex responses that would demonstrate appropriate levels of sensitivity and specificity for an electrodiagnostic test of LBP have not been established. Operant conditioning of H-reflex responses as targeted neuroplasticity of the Ia afferent-alpha motoneuron pathway improved spastic gait parameters.[33-35] However, the rehabilitation protocol does not readily translate into a clinical application because it involved 30 to 36 training

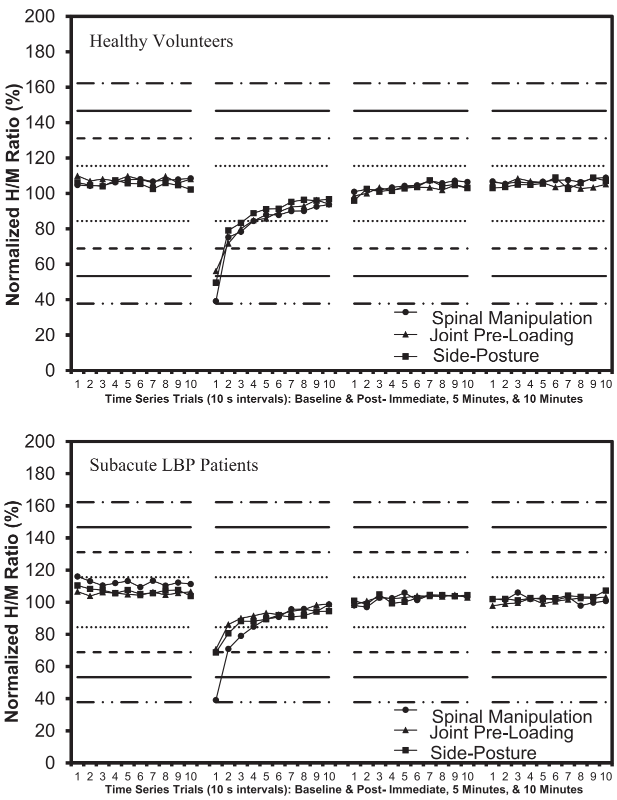

Fig 2. *Time series analysis of normalized H_{max}/M_{max} ratios for 10 trials evoked every 10 seconds before the lumbosacral procedure and at measurement time points immediately after and at 5 minutes and 10 minutes after the lumbosacral procedure: healthy volunteers and subacute LBP patients. LBP, low back pain.*

sessions, with each session consisting of 270 operant conditioning H-reflex trials during walking in a well-controlled research laboratory environment.[33-35] Thus, it seems unlikely that modulation of H-reflex responses to indicate targeted neuroplasticity of the Ia afferent-alpha motoneuron pathway would occur after SMT for patients with LBP.

However, using conditioning H-reflex protocols to measure changes in postactivation depression, reciprocal inhibition, presynaptic inhibition, and Renshaw cell inhibition within the Ia afferent-alpha motoneuron pathway may provide insights on neural adaptations that occur after SMT for patients with LBP.[24,25] Reliable and valid cat models that are being used to study the effects of SM on afferent discharges may be extended to study the mechanistic relationship among bistability properties of motoneuron membranes, hypertonicity, and SM-like loads.[19,36-39] Experimental models to induce and interrupt muscle cramps in humans may also provide insights on the mechanistic relationship among bistability properties of motoneuron membranes from motor unit discharge rates, hypertonicity, and HVLA SM.[40-42] Developing H-reflex methodologies as a translational tool for large-scale clinical research to measure the reliability of delivering the HVLA SM thrust and addressing the neuroplasticity that underlies SMT-induced pain relief and functional recovery for patients with LBP should be the focus of future research. In agreement with this future research direction, there is recent preliminary evidence that modulation of somatosensory-evoked potentials occurs as a neural correlate of pain reduction after 12 weeks of chiropractic care in 6 patients with chronic neck pain or upper limb pain.[43] Furthermore, the clinical utility of single-trial H-reflex responses for intraoperative monitoring of spinal nerve root function has been addressed in the literature.[44]

Limitations

The several limitations of this research included the following: (1) the potential for trial-to-trial variability of H-reflexes, (2) the side-lying HVLA SM procedure involving a large postural perturbation, (3) different sizes of the test H-reflex across participants, (4) recording tibial nerve H-reflexes from the GM, and (5) inferring neurophysiological effects of an HVLA SM thrust to the lumbosacral spine from a segmentally related muscle. The time series analysis, reliability indices, standard errors of measurements, consistency of stimulating and recording environments, and our experimental design to include SM control procedures indicated that H_{max}/M_{max} ratios recorded before and after the lumbosacral procedures were reliable, and the amount of H-reflex inhibition was dependent upon the L5-S1 HVLA SM. These data indicated that the time series analysis of H_{max}/M_{max} ratios, even in the presence of a large postural perturbation, documented a reliable and valid neurophysiological response to the L5-S1 HVLA SM thrust in the segmentally related GM. The nonspecific effects of movement or position artifacts on the H_{max}/M_{max} ratio were present, but nonspecific effects were not the main contributor to decreased H_{max}/M_{max} ratios after HVLA SM. There was a moderate inverse correlation (r = –.44) between the size of the H_{max}/M_{max} ratio at baseline (42.3% ± 14.29%, range: 19.26%-68.47%) and the amount of inhibition at the 10-second time point after an HVLA SM procedure among the patients with subacute LBP. However, inhibition of the H_{max}/M_{max} ratio at the 10-second post time point occurred in all patients with subacute LBP who underwent the HVLS SM procedure. Furthermore, the distributions of H_{max}/M_{max} ratios at baseline were similar between the patients with subacute LBP and healthy volunteers and across lumbosacral procedures. In addition, the interval of time between the last spinal treatment and HVLA SM for patients with subacute LBP and their enrollment into the study is a potential confounding variable.

Future research on the development of H-reflex methodologies as the neurophysiological indicator of a "successful" HVLA SM treatment may consider recording H-reflexes from the soleus muscle, standardizing the test reflex size across participants to 25% of M_{max},[45] or measuring the area under the curve of the H/M recruitment curve.[2] Measurements of soleus H-reflex in side-lying posture may also be considered.[8] The addition of a clinical researcher with credentials in the field of electrodiagnosis addresses the feasibility of including H-reflex methodology as a translational tool for large-scale clinical research to measure the reliability of delivering the HVLA SM thrust. However, given that there are multiple treatment sessions with HVLA SM in large-scale clinical research, the logistics of including H-reflex testing within a treatment session would need to be addressed.

Conclusion

Inhibition of the Ia afferent-alpha motoneuron pathway is a unique stimulus-response characteristic of HVLA SM that occurs in both asymptomatic adults and patients with subacute LBP. Beyond movement and position artifacts and trial-to-trial variability of H-reflex responses, a reliable and valid attenuation of H_{max}/M_{max} ratio occurred after L5-S1 HVLA SM.

Funding Sources and Conflicts of Interest

Funding support in part was received from the now defunct Foundation for Chiropractic Education and Research. No conflicts of interest were reported for this study.

Contributorship Information

Concept development (provided idea for the research): J. D.D., J.R.B.
Design (planned the methods to generate the results): J. D.D., J.R.B.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): J.D.D., J.R.B.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): J. D.D., J.R.B., P.D.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): J.R.B.
Literature search (performed the literature search): J.D. D., J.R.B., P.D.
Writing (responsible for writing a substantive part of the manuscript): J.D.D., J.R.B.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): J.D.D., J.R.B.

Practical Applications

- The data provide insights on the unique stimulus-response characteristics of delivering HVLA SM thrust to the lumbosacral spine in human participants.
- High-velocity, low-amplitude spinal manipulation thrusts inhibit the excitability of lumbosacral motoneurons.
- The data add value to the existing evidence by including SM control procedures and a patient population: patients with subacute LBP.
- Attenuation of lumbosacral motoneuron excitability by HVLA SM thrusts is a potential mechanism to alleviate hypertonicity that may be associated with LBP or detected with palpation.

References

1. Dishman JD, Weber KA, Corbin RL, Burke JR. Understanding inhibitory mechanisms of lumbar spinal manipulation using H-reflex and F-wave responses: a methodological approach. *J Neurosci Methods.* 2012;210(2):169-177.
2. Niazi IK, Turker KS, Flavel S, Kinget M, Duehr J, Haavik H. Changes in H-reflex and V-waves following spinal manipulation. *Exp Brain Res.* 2015;233(4):1165-1173.
3. Bulbulian R, Burke J, Dishman JD. Spinal reflex excitability changes after lumbar spine passive flexion mobilization. *J Manipulative Physiol Ther.* 2002;25(8):526-532.
4. Burke JR, Bulbulian R. Modulation of the tibial nerve H-reflex by mechanical stimulation of afferents in the lumbar spine. *Electromyogr Clin Neurophysiol.* 2005;45(2):105-113.
5. Dishman JD, Bulbulian R. Comparison of effects on spinal manipulation and massage on motoneuron excitability. *Electromyogr Clin Neurophysiol.* 2001;41(2):97-106.
6. Dishman JD, Cunningham BM, Burke J. Comparison of tibial nerve H-reflex excitability after cervical and lumbar spine manipulation. *J Manipulative Physiol Ther.* 2002;25(5):318-325.
7. Dishman JD, Dougherty PE, Burke JR. Evaluation of the effect of postural perturbation on motoneuronal activity following various methods of lumbar spinal manipulation. *Spine J.* 2005;5(6):650-659.
8. Suter E, McMorland G, Herzog W. Short-term effects of spinal manipulation on H-reflex amplitude in healthy and symptomatic subjects. *J Manipulative Physiol Ther.* 2005;28(9):667-672.
9. Murphy BA, Dawson NJ, Slack JR. Sacroiliac joint manipulation decreases the H-reflex. *Electromyogr Clin Neurophysiol.* 1995;35(2):87-94.

10. Herzog W, Scheele D, Conway PJ. Electromyographic responses of back and limb muscles associated with spinal manipulative therapy. *Spine (Phila Pa 1976).* 1999;24(2):146-152.
11. Page I, Nougarou F, Descarreaux M. Neuromuscular response amplitude to mechanical stimulation using large-array surface electromyography in participants with and without chronic low back pain. *J Electromyogr Kinesiol.* 2016;27:24-29.
12. Dishman JD, Ball KA, Burke J. First prize: central motor excitability changes after spinal manipulation: a transcranial magnetic stimulation study. *J Manipulative Physiol Ther.* 2002;25(1):1-9.
13. Dishman JD, Greco DS, Burke JR. Motor-evoked potentials recorded from lumbar erector spinae muscles: a study of corticospinal excitability changes associated with spinal manipulation. *J Manipulative Physiol Ther.* 2008;31(4):258-270.
14. Haavik H, Niazi IK, Jochumsen M, Sherwin D, Flavel S, Turker KS. Impact of spinal manipulation on cortical drive to upper and lower limb muscles. *Brain Sci.* 2016;7(1):E2.
15. Daligadu J, Haavik H, Yielder PC, Baarbe J, Murphy B. Alterations in cortical and cerebellar motor processing in subclinical neck pain patients following spinal manipulation. *J Manipulative Physiol Ther.* 2013;36(8):527-537.
16. Taylor HH, Murphy B. Altered sensorimotor integration with cervical spine manipulation. *J Manipulative Physiol Ther.* 2008;31(2):115-126.
17. Lelic D, Niazi IK, Holt K, Jochumsen M, Dremstrup K, Yielder P, et al. Manipulation of dysfunctional spinal joints affects sensorimotor integration in the prefrontal cortex: a brain source localization study. *Neural Plast.* 2016;20163704964.
18. Cao DY, Reed WR, Long CR, Kawchuk GN, Pickar JG. Effects of thrust amplitude and duration of high-velocity, low-amplitude spinal manipulation on lumbar muscle spindle responses to vertebral position and movement. *J Manipulative Physiol Ther.* 2013;36(2):68-77.
19. Reed WR, Cao DY, Long CR, Kawchuk GN, Pickar JG. Relationship between biomechanical characteristics of spinal manipulation and neural responses in an animal model: effect of linear control of thrust displacement versus force, thrust amplitude, thrust duration, and thrust rate. *Evid Based Complement Alternat Med.* 2013;2013492039.
20. Reed WR, Long CR, Kawchuk GN, Pickar JG. Neural responses to the mechanical parameters of a high-velocity, low-amplitude spinal manipulation: effect of preload parameters. *J Manipulative Physiol Ther.* 2014;37(2):68-78.
21. Reed WR, Long CR, Kawchuk GN, Sozio RS, Pickar JG. Neural responses to physical characteristics of a high velocity, low amplitude spinal manipulation: effect of thrust direction. *Spine.* 2018;43(1):1-9.
22. Herzog W. The biomechanics of spinal manipulation. *J Bodyw Mov Ther.* 2010;14(3):280-286.
23. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
24. Pierrot-Deseilligny E, Mazevet D. The monosynaptic reflex: a tool to investigate motor control in humans. Interest and limits. *Neurophysiol Clin.* 2000;30(2):67-80.
25. Knikou M. The H-reflex as a probe: pathways and pitfalls. *J Neurosci Methods.* 2008;171(1):1-12.
26. Klimstra M, Zehr EP. A sigmoid function is the best fit for the ascending limb of the Hoffmann reflex recruitment curve. *Exp Brain Res.* 2008;186(1):93-105.
27. Alrowayeh HN, Sabbahi MA, Etnyre B. Similarities and differences of the soleus and gastrocnemius H-reflexes during varied body postures, foot positions, and muscle function: multifactor designs for repeated measures. *BMC Neurol.* 2011;11:65.
28. Hultborn H, Nielsen J. Modulation of of transmitter release from Ia afferents by their preceding activity - a ”post activation depression”. In: Rudomin P, Romo R, Mendell L, eds. Presynaptic Inhibition and Neural Control. Oxford, UK: Oxford University Press; 1998. p. 178-191.
29. Shekelle PG, Coulter I, Hurwitz EL, Genovese B, Adams AH, Mior SA, et al. Congruence between decisions to initiate chiropractic spinal manipulation for low back pain and appropriateness criteria in North America. *Ann Intern Med.* 1998;129(1):9-17.
30. Dishman JD, Bulbulian R. Transient suppression of alpha motoneuron excitability following lumbosacral spinal manipulation. *Spine.* 2000;25:2519-2525.
31. Dishman JD, Cunningham BM, Burke JR. Effects of regional and non-regional spinal manipulation on motoneuron excitability. *J Manipulative Physiol Ther.* 2002;25:318-325.
32. Dishman JD, Burke J. Spinal reflex excitability changes after cervical and lumbar spinal manipulation: a comparative study. *Spine J.* 2003;3(3):204-212.
33. Thompson AK, Chen XY, Wolpaw JR. Soleus H-reflex operant conditioning changes the H-reflex recruitment curve. *Muscle Nerve.* 2013;47(4):539-544.
34. Thompson AK, Wolpaw JR. Targeted neuroplasticity for rehabilitation. *Prog Brain Res.* 2015;218:157-172.
35. Thompson AK, Wolpaw JR. Restoring walking after spinal cord injury: operant conditioning of spinal reflexes can help. *Neuroscientist.* 2015;21(2):203-215.
36. Bolton PS, Budgell BS. Spinal manipulation and spinal mobilization influence different axial sensory beds. *Med Hypotheses.* 2006;66(2):258-262.
37. Edgecombe TL, Kawchuk GN, Long CR, Pickar JG. The effect of application site of spinal manipulative therapy (SMT) on spinal stiffness. *Spine J.* 2015;15(6):1332-1338.
38. Eken T, Hultborn H, Kiehn O. Possible functions of transmitter-controlled plateau potentials in alpha motoneurones. *Prog Brain Res.* 1989;80:257-267.
39. Pickar JG. Neurophysiological effects of spinal manipulation. *Spine J.* 2002;2(5):357-371.
40. Baldissera F, Cavallari P, Dworzak F. Cramps: a sign of motoneurone ’bistability’ in a human patient. *Neurosci Lett.* 1991;133(2):303-306.
41. Baldissera F, Cavallari P, Dworzak F. Motor neuron ’bistability’. A pathogenetic mechanism for cramps and myokymia. *Brain.* 1994;117(Pt 5):929-939.
42. Minetto MA, Holobar A, Botter A, Farina D. Origin and development of muscle cramps. *Exerc Sport Sci Rev.* 2013;41(1):3-10.
43. Haavik H, Niazi IK, Holt K, Murphy B. Effects of 12 weeks of chiropractic care on central integration of dual somatosensory input in chronic pain patients: a preliminary study. *J Manipulative Physiol Ther.* 2017;40(3):127-138.
44. Leppanen RE. Monitoring spinal nerve function with H-reflexes. *J Clin Neurophysiol.* 2012;29(2):126-139.
45. Crone C, Hultborn H, Mazieres L, Morin C, Nielsen J, Pierrot-Deseilligny E. Sensitivity of monosynaptic test reflexes to facilitation and inhibition as a function of the test reflex size: a study in man and the cat. *Exp Brain Res.* 1990;81(1):35-45.