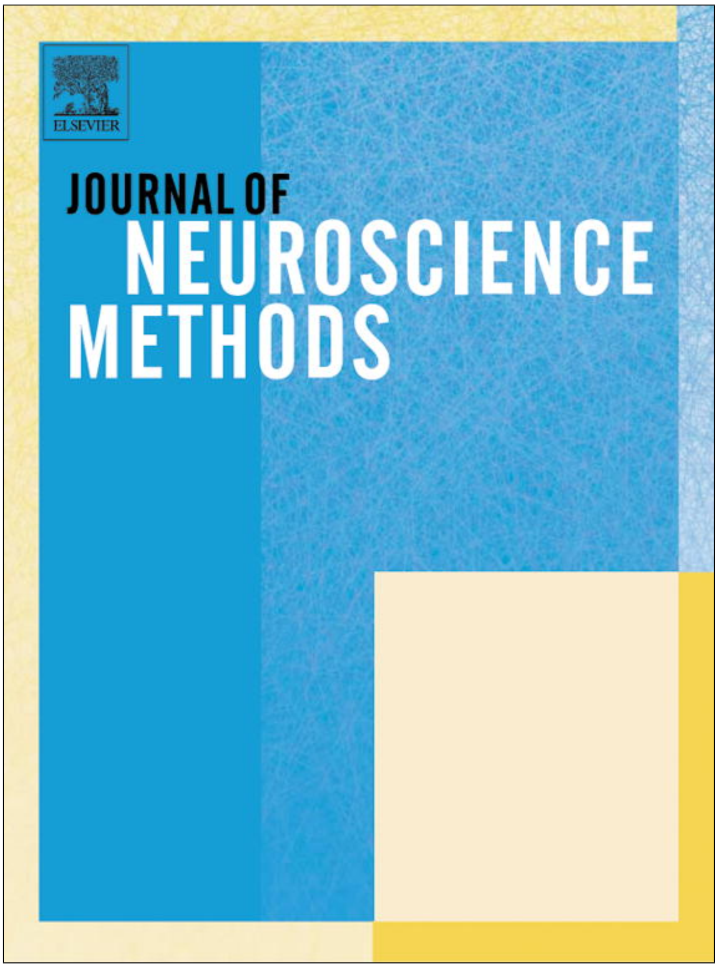
ELSEVIER
JOURNAL OF
NEUROSCIENCE
METHODS

Journal of Neuroscience Methods 210 (2012) 169–177

Contents lists available at SciVerse ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Clinical Neuroscience

Understanding inhibitory mechanisms of lumbar spinal manipulation using H-reflex and F-wave responses: A methodological approach

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HIGHLIGHTS

- H-reflex is reliably attenuated following spinal manipulation.
- H-reflex attenuation is sensitive and unique to manipulation.
- H-reflex is a reliable index of motor neuron excitability.
- F-wave responses are not sensitive to mechanical perturbation of the spine.

ARTICLE INFO

Article history:
Received 7 April 2012
Received in revised form 13 July 2012
Accepted 23 July 2012

Keywords:
Lumbar manipulation
H-reflex
Time series analysis
Mechanical low back pain

ABSTRACT

The purpose of this research was to characterize unique neurophysiologic events following a high velocity, low amplitude (HVLA) spinal manipulation (SM) procedure. Descriptive time series analysis techniques of time plots, outlier detection and autocorrelation functions were applied to time series of tibial nerve H-reflexes that were evoked at 10-s intervals from 100 s before the event until 100 s after three distinct events L5-S1 HVLA SM, or a L5-S1 joint pre-loading procedure, or the control condition. Sixty-six subjects were randomly assigned to three procedures, i.e., 22 time series per group. If the detection of outliers and correlograms revealed a pattern of non-randomness that was only time-locked to a single, specific event in the normalized time series, then an experimental effect would be inferred beyond the inherent variability of H-reflex responses. Tibial nerve F-wave responses were included to determine if any new information about central nervous function following a HVLA SM procedure could be ascertained. Time series analyses of H_{max}/M_{max} ratios, pre–post L5-S1 HVLA SM, substantiated the hypothesis that the specific aspects of the manipulative thrust lead to a greater attenuation of the H_{max}/M_{max} ratio as compared to the non-specific aspects related to the postural perturbation and joint pre-loading. The attenuation of the H_{max}/M_{max} ratio following the HVLA SM procedure was reliable and may hold promise as a translational tool to measure the consistency and accuracy of protocol implementation involving SM in clinical trials research. F-wave responses were not sensitive to mechanical perturbations of the lumbar spine.

1. Introduction

Low back and neck pain are the fifth most expensive health condition in the United States (Druss et al., 2002). Although the economic cost of back pain has been estimated at 83 million loss work days and $12 billion annually (Druss et al., 2002), epidemiological data have shown that spinal pain conditions are on the rise (Louw et al., 2007; Freburger et al., 2009). Evidence-informed management of neck and low back pain includes spinal manipulative therapy (SMT) (Bronfort et al., 2004, 2008; Haldeman and Dagenais, 2008; Hurwitz et al., 2008; Lawrence et al., 2008). A systematic review of clinical practice guidelines recommend that history, physical examination and neurological examination are sufficient to identify 99% of potentially serious spinal pathology or specific causes of low back pain in which advanced diagnostic testing and interventions are appropriate (Dagenais et al., 2010a). Cost-effective conservative approaches to include SMT are appropriate for the vast majority of patients with recurring, non-life-threatening low back pain seen in the primary care setting (Haas et al., 2005; Mayer et al., 2010; Dagenais et al., 2010a,b; Lin et al., 2011a,b).

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http://dx.doi.org/10.1016/j.jneumeth.2012.07.014

However, methods need to be developed to measure the consistency and accuracy of protocol implementation involving SMT in large-scale clinical research. The development of reliable and valid translational tools for large-scale clinical research will enhance our abilities to collect the quality and quantity of evidence needed to more definitely address the clinical efficacy and cost-effectiveness of SMT for spine syndromes (Korthals-de Bos et al., 2003; Herman et al., 2005; Hurwitz et al., 2008; Dagenais et al., 2010a; Rubinstein et al., 2011; Lin et al., 2011b). The majority of evidence to date, in both human and animal models, indicates that SMT may regulate afferent discharges that appear to be dependent on the types of manipulative thrusts and vertebral loading applied to the spine (Murphy et al., 1995; Bolton and Holland, 1998; Pickar, 1999, 2002; Dishman et al., 2005; Sung et al., 2005; Bolton and Budgell, 2006; Pickar et al., 2007). A time series of tibial nerve H-reflex trials (Dishman et al., 2005; Suter et al., 2005) or pre–post H/M recruitment curves (Murphy et al., 1995) have been analyzed to address the unique stimulus–response characteristics of high velocity, low amplitude (HVLA) spinal manipulation (SM) procedures on the Ia afferent – alpha motoneuron pathway. The amount of attenuation of the H_{max}/M_{max} ratio following a HVLA SM procedure as compared to control conditions may be a translational tool to measure the consistency and accuracy of protocol implementation involving SMT in large-scale clinical research. As a translational tool, methodological considerations need to be addressed because the measurements of H-reflexes may be confounded by many factors (Pierrot-Deseilligny and Mazevet, 2000; Misiaszek, 2003; Knikou, 2008).

When the tibial nerve H-reflex amplitude was normalized to maximal M-wave amplitude to allow for proper comparison across experimental conditions (Crone et al., 1990), a reliable and consistent attenuation of H_{max}/M_{max} ratio occurred as a specific aspect of L5-S1 HVLA SM (Murphy et al., 1995; Dishman and Bulbulian, 2000, 2001; Dishman et al., 2002, 2005; Dishman and Burke, 2003). Following L5-S1 HVLA SM, the non-specific effects of movement/position artifacts on the H_{max}/M_{max} ratio are present, but unlike, when normalizing H-reflex amplitudes to a percentage of the control H-reflex amplitude, the effect of postural perturbation, or body positioning, is not the main contributor to decreased H-reflex amplitude (Dishman et al., 2005; Suter et al., 2005). In addition, heteronymous conditioning effects from mechanical stimulations of Groups I–IV afferents of the lumbar spine during passive trunk movements attenuate tibial nerve H-reflexes recorded from the segmentally related gastrocnemius muscle (Burke and Bulbulian, 2005). What remains problematic in the use of the H_{max}/M_{max} ratio as a translational tool is that the side-lying HVLA SM procedure involves a large postural perturbation that can only be safely applied once within the experimental session (Triano et al., 2002, 2003; Van Zoest and Gosselin, 2003). A postural perturbation is one of many factors that may affect the amplitude of the H-reflex response (Pierrot-Deseilligny and Mazevet, 2000; Misiaszek, 2003; Knikou, 2008).

Previous research on the neurophysiologic effects of HVLA SM (cf. Murphy et al., 1995; Dishman et al., 2005) was able to address the potential confounders underlying H-reflex methodology (Crone et al., 1990, 1999; Hultborn and Nielsen, 1998; Pierrot-Deseilligny and Mazevet, 2000; Misiaszek, 2003; Klimstra and Zehr, 2008; Knikou, 2008) by documenting that the recording and stimulating environments and the relative thresholds of Ia afferents and motor axons were constant before and after the experimental and control perturbations. However, measuring the acute time course of changes in H_{max}/M_{max} ratios following a L5-S1 HVLA SM from single trials of tibial nerve H-reflexes across multiple subjects may seem questionable due to the inherent variability of H-reflex responses across individual trials (Pierrot-Deseilligny and Mazevet, 2000; Misiaszek, 2003; Knikou, 2008). A time series analysis of single trial H-reflexes averaged across multiple subjects under different experimental conditions may differentiate an unique stimulus–response pattern from a random distribution of trial-to-trial variability in neurophysiologic responses (Truccolo et al., 2002). Relative and absolute indices to measure the reliability of H_{max}/M_{max} ratios from triceps surae muscles across individual trials indicate adequate reliability (Alrowayeh and Sabbahi, 2009; Hoch and Krause, 2009; Alrowayeh et al., 2011). Although the sensitivity to inhibition and facilitation of H_{max}/M_{max} ratios may be influenced by the proportion of motoneurons participating in the H-reflex response, i.e., variations among subjects in the sizes of their H_{max}/M_{max} ratios, any potential confounder of test reflex size can be addressed by data analysis (Crone et al., 1990; Klimstra and Zehr, 2008; Hoch and Krause, 2009).

The purpose of this research was to characterize unique neurophysiologic events following a HVLA SM procedure at intervals of measurements that were significantly different from some underlying baseline variability and the non-specific aspects of delivering the HVLA SM procedure. Descriptive time series analysis techniques of time plots, outlier detection and autocorrelation functions were applied to time series of tibial nerve H-reflexes that were evoked at 10-s intervals from 100 s before the event until 100 s after three distinct events L5-S1 HVLA SM, or a L5-S1 joint preloading procedure, or the control condition. Sixty-six subjects were randomly assigned to three procedures, i.e., 22 time series per experimental condition. If the detection of outliers and correlograms revealed a pattern of non-randomness that was only time-locked to a single, specific event in the normalized time series, then an experimental effect would be inferred beyond the inherent variability of H-reflex responses. Tibial nerve F-wave responses were included in the current study to determine if any new information about central nervous function following a HVLA SM procedure could be ascertained (Mesrati and Vecchierini, 2004; Fisher, 2007).

2. Material and methods

2.1. Participants

A convenience sample of 66 healthy male and female volunteers between the ages of 20 and 50 years old were recruited from the local campus community to participate in the research (Table 1). All procedures were approved by the local institutional review board and complied with the declaration of Helsinki. Written informed consent was obtained from all participants. Subjects had no past history of peripheral neuropathy or radiculopathy and were free from any subjective complaints of low back pain for a period of 48 h prior to participation in the study.

2.2. Experimental design

The quasi-experimental, laboratory controlled design used time series analyses and random assignment of subjects into three groups to address the specific and non-specific aspects of a side-posture L5-S1 HVLA thrust on alpha motoneuron excitability via Ia afferent – alpha motoneuron pathway (H-reflex) and the antidromic alpha motor axon pathway (F-response). The three groups were: (1) time series control, (2) pre–post time series pattern of responses for side-posture positioning with L5-S1 joint pre-loading, and (3) pre–post time series pattern of responses for side-posture positioning with joint pre-loading and the delivery of the L5-S1 HVLA thrust. Using a prone testing position, H-reflex and F-response recordings were obtained by tibial nerve stimulation and recorded from the gastrocnemius and abductor hallucis muscles, respectively, in two experimental sessions separated by

Table 1
Characteristics of the participants (means ± standard deviations).

Groups	Gender	Age (years)	Height (cm)	Weight (kg)
Time series control	17 males 5 female	27.1 ± 4.57	177.5 ± 9.12	77.8 ± 15.08
Joint pre-loading	16 males 6 females	29.7 ± 6.83	175.6 ± 8.56	77.2 ± 13.66
HVLA SM	15 males 7 females	26.5 ± 4.19	174.1 ± 7.51	78.1 ± 14.82

a minimum of 48 h. All subjects were randomized as to whether H-reflexes or F-responses were recorded in the first experimental session to avoid order effects. The time series analysis incorporated 10 baseline recordings of H-reflexes or F-responses prior to the procedure, L5-SI HVLA SM, L5-S1 joint pre-loading, or time control, and then ten subsequent recordings of H-reflexes or F-responses, post-procedure. Changes in the time series patterns, pre–post procedures, were used to determine the specific and non-specific aspects of a side-posture L5-S1 HVLA thrust on alpha motoneuron excitability.

2.3. H-reflex methodology

2.3.1. Recording and stimulation procedures

The standardization of electrode placement for recording M-waves and H-reflexes from the medial head of the gastrocnemius muscle (GM) across subjects was according to electrodiagnostic methodology initially described by Braddom and Johnson (1974) and DeLisa et al. (1994). These electromyographic (EMG) responses were recorded from the right leg using 10 mm bipolar self-adhesive, pre-gelled, surface disposable Ag–AgCl electrodes. The active electrode was placed over the medial head of the GM at the midpoint distance on a line measured between the midpopliteal crease and the most proximal part of medial malleolus. The reference electrode was placed over the Achilles tendon, midline, at the level of the medial malleolus with the ground electrode at the midpoint distance on a line measured between the midpopliteal crease and inferior margins of the medial and lateral heads of the GM along the midline. EMG signals were bandpass filtered (10 Hz–1 kHz) in accordance with electrodiagnosis standards for recording M-wave and H-reflex evoked potentials (Kimura, 2001) and amplified using PC-based EMG instrument (Cadwell Wave, Cadwell Laboratories, Kennewick, WA, USA). Peak-to-peak EMG amplitudes of M-wave and H-reflex responses were recorded for data analyses. The right tibial nerve was stimulated in the popliteal fossa using a 1.0 ms square wave pulse delivered by a constant current stimulator, 0–100 mA through a bipolar electrode configuration (Cadwell Wave, Cadwell Laboratories, Kennewick, WA, USA).

2.3.2. H/M recruitment curve and size of the test H-reflex

Prior to generating the time series of H-reflex responses, the standard *H*/*M* recruitment curve was generated with the subject prone on a treatment table and with their feet secured to a plate to maintain a 90° angle of the foot to the tibia (Pierrot-Deseilligny and Mazevet, 2000; Knikou, 2008; Klimstra and Zehr, 2008; Alrowayeh et al., 2011). The stimulus intensity was then adjusted to evoke the maximum H-reflex response that was verified to occur at the apex of the ascending portion of the H-reflex recruitment curve (Pierrot-Deseilligny and Mazevet, 2000; Knikou, 2008; Klimstra and Zehr, 2008). This stimulus intensity also evoked a submaximal M-wave response with the maximal H-reflex response, which was visually monitored to ensure the consistency of the stimulating and recording environments across trials during the test session, i.e., constant stimulus intensity and no impedance changes or electrode movement at the stimulating or recording sites. Before and after the control condition and perturbation procedures, a time series of 10 H-reflexes were recorded at rate of 0.1 Hz. The rate of 0.1 Hz avoided post-activation depression of H-reflexes (Hultborn and Nielsen, 1998). The size of the test H-reflex, maximum H-reflex response, was expressed relative to the maximum M-wave. 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.

2.3.3. Time series analyses

The dependent variable was the H_{max}/M_{max} ratio. The following normalization procedure was applied to the data of each subject. The mean of the 20 trials in the time series, pre–post procedure, was calculated. Then, each trial in the time series was expressed as percent of the mean of H_{max}/M_{max} ratio with 100% representing the mean H_{max}/M_{max} ratio for the 20 trials in the time series. For event detection, the average standard deviation (SD) of the normalized time series data from all 66 subjects was calculated. Within each group, time series plots of the normalized data for each of the 22 subjects were generated with an event bar at ±3 SD units to detect the number of unique events at each time point per experimental condition. To confirm the robustness of the detected outliers, the Tukey's method, constructing a boxplot, was applied at time points where the standard deviation method detected unique events. Mean time series plots for each group with event bars at ±1, 2, 3 and 4 SD units were generated to compare the occurrences of unique events among experimental conditions at each time point.

Autocorrelation coefficients were calculated across all subjects whose data sets were organized by subject number (1–22) and experimental condition (1–3) at each 10 s time point (±100 s of the control and perturbation procedures). The underlying assumption was that the observed time series per subject was just one sample of an infinite set of time series that might have been observed. Within this data management structure, autocorrelation coefficients predominately measured correlations between *H*/*M* responses within groups at lags ≤7 and between groups at lags >7 at each time point. Events at each time point were purely random if autocorrelation coefficients fell within the 95% confidence limits, $\pm 2\sqrt{N}$. A pattern of autocorrelation coefficients outside the "null" 95% confidence limits, based upon the interpretations of size and lag, indicated non-randomness, i.e., a significant event at a time point.

2.4. F-wave methodology

2.4.1. Recording and stimulation procedures

All EMG recordings and tibial nerve stimulations were performed using the Cadwell Wave EMG instrument (Cadwell Laboratories, Kennewick, WA, USA). Electrodiagnostic methodology was followed to ensure the consistent placement of electrodes for recording F-waves from the right abductor hallucis (AB) muscle across subjects (Kimura, 2001; Mesrati and Vecchierini, 2004). F-wave responses were recorded by placing a self-adhesive 10 mm Ag/AgCl recording electrode (Neuroline, Slovunde, Denmark) over the midpoint of the right AH muscle just inferior to the prominence of the navicular bone. An additional 10 mm self-adhesive Ag/AgCl electrode was placed as a reference more distally over the lateral aspect of the first metatarsal head and another 10 mm electrode was placed on the medial malleolus as a ground. EMG signals were amplified and bandpass filtered (10 Hz–1 kHz) in accordance with electrodiagnosis standards for recording F-wave evoked potentials (Kimura, 2001; Mesrati and Vecchierini, 2004).

The right tibial nerve was stimulated using 0.1 ms square wave pulse that was delivered by a constant current stimulator, 0–100 mA, through a bipolar electrode configuration that was placed posterior and inferior to the medial malleolus (Mesrati and Vecchierini, 2004). The stimulus intensity was increased until the amplitude of the compound muscle action potential, M-wave, evoked from the AH muscle did not increase with three subsequent increases in stimulus intensity. That final stimulus intensity was deemed the supramaximal stimulus intensity for the F-wave study. Pre–post procedure, the right tibial nerve was stimulated supramaximally using a train of 10 stimuli at a frequency of 1 Hz. EMG peak-to-peak amplitude and persistence of the 10 F-wave responses were recorded, pre–post procedure. Before and after the F-wave study, EMG peak-to-peak amplitudes of the maximum M-wave responses at the supramaximal stimulus intensity were recorded to verify that impedance changes or electrode movement at the stimulating or recording sites did not occur.

2.4.2. Data and time series analyses

From the literature, the persistence of the tibial nerve F-wave from the AH is 97 ± 5% with minimum, mean and maximum latencies of 47 ± 4.3 ms, 49.6 ± 4.4 ms to 52.5 ± 4.4 ms, respectively and mean amplitude of 384 ± 148 μV (Nobrega et al., 2004). In the current study, persistence of the tibial nerve F-wave from the AH was 98.7 ± 4.35% with a mean latency of 49.7 ± 4.42 ms and a mean amplitude of 420 ± 329 μV, which confirms the validity of the F-wave data. The threshold of amplitude to detect the presence of a F-wave was 20 μV. On the limited number of trials when a F-wave was not presence or <20 μV, 0 μV was recorded. For the time series analysis, the dependent variable was the F-wave amplitude. The normalized time series analyses were the same as described for the H-reflex responses. In addition to normalized time series analysis, a time series plot of the F-wave amplitudes in μV was also depicted.

2.5. Control and perturbation procedures

2.5.1. Control procedure

The control group subjects remained prone on the treatment table during the whole experimental session and were not subject to any perturbation. A time series of ten test responses were recorded, and then after 30 s, a second time series of ten test responses were recorded. This time series replicated the time course of evoking test responses for subjects assigned to receive either the L5-S1 HVLA SM procedure or the L5-S1 joint pre-loading procedure.

2.5.2. L5-S1 HVLA SM procedure

A time series of ten test responses were recorded with the subject resting prone on the treatment table. Then, subjects were administered a HVLA side-lying L5-S1 SM procedure as commonly performed by practitioners of chiropractic and osteopathy that was applied ipsilateral to the side of test responses (right side). After positioning the subject into a side-lying posture, the clinician provided a manual contact upon the tissues overlying the lumbar zygapophysial joints. The soft tissue tension was slightly increased by providing +*Y*-axis translation (distraction) to the spine, coupled with a ±*Y*-axis rotation force, thereby increasing the mechanical load upon the soft tissues. Once tissue tension was maximized, a HVLA impulsive force was applied. The primary force vector was +*Z*-axis translation, with a secondary vector consisting of ±*Y*-axis rotation. Upon completion of the procedure, the subjects were immediately returned to the prone testing position and a post time series of ten test responses were recorded. There were ≈30 s between the pre and post time series recordings.

2.5.3. L5-S1 joint pre-loading procedure

The intention of the joint pre-loading procedure was to accurately replicate the side-posture L5-S1 SM procedure with the exception of the application of the HVLA thrust. In the L5-S1 joint pre-loading procedure, manual contact was applied to the joints of the lumbosacral spine; however, no thrust was applied. Other than the absence of a manipulative thrust, the joint pre-loading procedure did not differ from the L5-S1 HVLA SM procedure.

2.6. Statistical analyses

Event detection from the time series plots was the primary statistical analysis, which included outlier detection and autocorrelation functions. Secondary analyses included the calculations of intraclass correlation coefficients (ICC) and a Group × Time mixed ANCOVA model. ICCs were used to determine the reliabilities of the data responses and post-procedural effects. For the post-procedural effects, the normalized data response at the 10 s post-procedure time point from the 22 subjects per group were randomly organized into seven sets of three trials of data responses. This was accomplished by using a random generator to organize the data from the 22 subjects per group into seven sets of three trials. Five data sets were created consisting of 21 sets of three trials using the outputs of the random generator from each group. Another two data sets of 21 sets of three trials were created by (1) sorting the normalized data response at the 10 s post-procedure time point from high to low and again from low to high within each group, (2) organizing each of the two sorted data responses into seven sets of three trials per group and then (3) merging outputs from the three groups by sort order.

To confirm the time series analyses, a Group × Time mixed ANCOVA model was used to reveal changes in H_{max}/M_{max} ratios and F-wave responses, pre–post procedure. For the H_{max}/M_{max} ratio (absolute), F-wave amplitude (μV), and F-wave latency (ms), the baseline mean was calculated from the 10 pre-procedure trials and used as a covariate to account for slight variations among the three experimental groups. The Dunnett's post hoc test was used to detect changes within each experimental group across time from 10 s to 60 s, post-procedure with respect to the baseline value. The Student Newman–Keuls post hoc test was used to detect changes among the experimental groups at each measurement time point. The level of significance was .05, and SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for all statistical procedures.

3. Results

3.1. Consistency of the stimulating and recording environments

In both testing sessions, maximum M-wave amplitudes were similar pre (24.1 ± 6.44 mV) and post (23.9 ± 6.21 mV) procedures ($p > 0.05$). The submaximal M-waves on the H-reflex trials were consistent as visually observed on each data trace collected as part of the time series.

3.2. H-reflex responses

The ICC values for H_{max}/M_{max} ratios within each group during the time series were .99. Mean coefficients of variations among the subjects were between 4.0% and 6.0%. Immediate post-procedure at the 10 s time point, event detection, >3 SD, occurred in 15 of 22

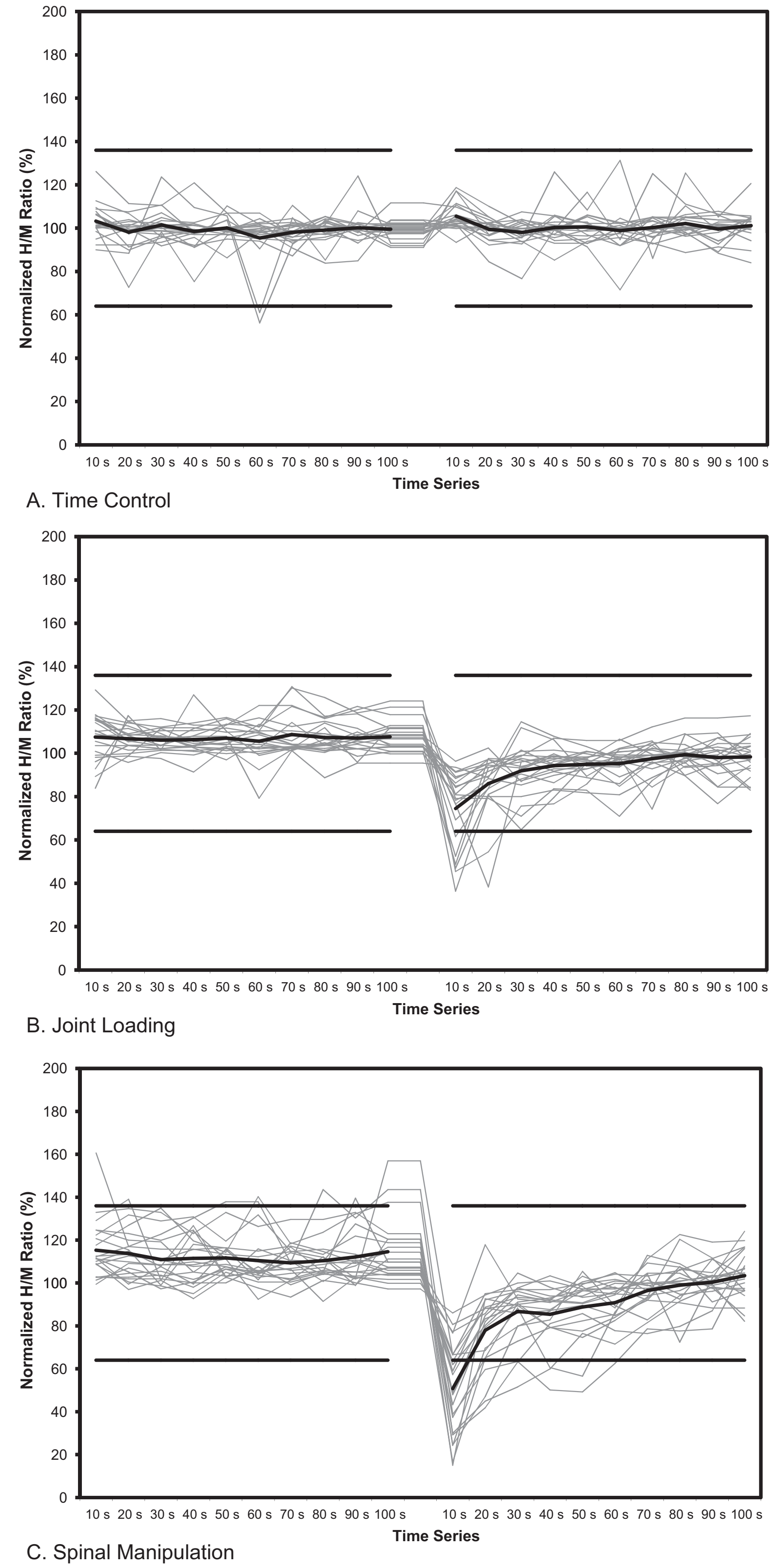

Fig. 1. Time series analysis for each of the experimental conditions: (A) time control; (B) L5-S1 joint pre-loading; and (C) L5-S1 HVLA SM. The gray lines in each panel represent the time series for each subject within each experimental condition. The time series reflects 20 neurophysiologic responses to three distinct events, from 100 s before the event until 100 s after the event at 10-s intervals. The pre–post event time series is joined by a straight line for each subject. The upper and lower straight lines (black) are the event bars at ±3 SD units to detect the number of unique events at each time point per experimental condition. The center black line in each panel is the averaged time series of the subjects in each experimental condition. The time series of the normalized H-reflex responses for each subject, within each of the experimental conditions, reflects a random pattern of trial-to-trial variability for the subjects in the control group and receiving the L5-S1 joint pre-loading procedure; whereas, there is a distinct spike of trial-to-trial variability at the 10 s time point, post-event, for the subjects receiving L5-S1 HVLA SM.

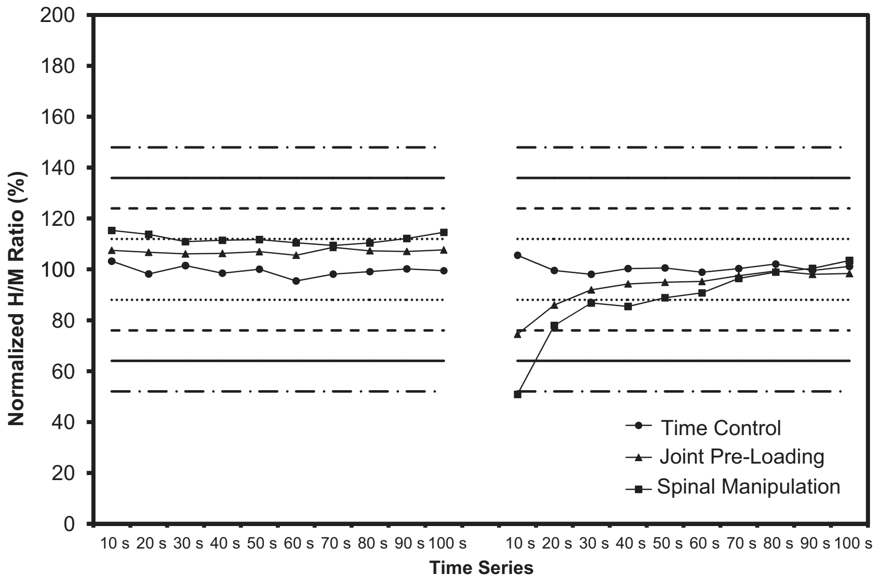

Fig. 2. The averaged time series for each of the experimental conditions: time control (●); L5-S1 joint pre-loading (▲); and L5-S1 HVLA SM (■). The four straight lines, paired upper and lower line patterns, are ±1 SD, 2 SDs, 3 SDs and 4 SDs. Comparing the averaged time series of the normalized H-reflex responses among the experimental groups indicated that mean responses at the 10 s time point were: (1) >4 SDs L5-S1 HVLA SM, (2) >2 SDs for the joint position group, and (3) within 1 SD for the control group.

subjects in the lumbar SM group, in only 6 of 22 subjects in the joint loading group and in none of subjects in time control group ($\chi^2_{df=2} = 23.9, p < .05$). Any events detected during the baseline time series and for the last nine trials were random and non-significant among the three groups. Using the first and three quadrants of the data distribution (Q_1 and Q_3), the interquartile range (IQR) and the detection of "extreme outliers" ($Q_1 - 3 \times$ IQR, $Q_3 + 3 \times$ IQR), the same number of events were detected with the Tukey method to confirm the robustness of our findings. Fig. 1 reflects the time series analysis within each group. Fig. 2 summarizes the between group time series analysis in which the mean responses at the 10 s time point were: (1) >4 SDs for the lumbar SM group, (2) >2 SDs for the joint position group; and (3) within 1 SD for the control group.

There was a significant Group by Time interaction for H/M_{max} ratio [$F_{(10,310)} = 17.77$, $p < .05$] (Fig. 3). At 10 s post-procedure, the magnitude of H_{max}/M_{max} ratio attenuation was greater following lumbar SM (49%) as compared to joint pre-loading (31%; $p < .05$) with an effect size of the spinal procedures accounting for the 56% of the variance in H_{max}/M_{max} ratio (partial eta squared = .56). Lumbar

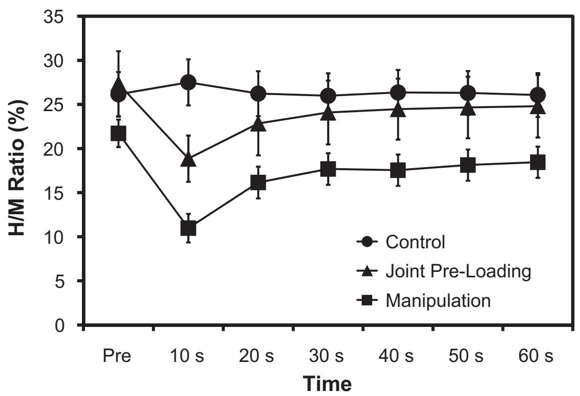

Fig. 3. Mean *H/M* ratios (±SE) over time. *H/M* ratios at 10-s intervals from 10 to 60 s following either L5-S1 HVLA SM (■) or L5-S1 joint pre-loading procedure (▲) as compared to baseline values, pre-procedure. In the control condition (●) with subjects lying prone, *H/M* ratios were recorded following a similar time course as for the experimental procedures. The "Pre" label refers to the mean ± SE of the 10 H-reflex trials before the experimental procedures or time control.

SM accounted for 39% of the variance in H_{max}/M_{max} ratio (partial eta squared = .39); whereas, joint pre-loading accounted for 29% of the variance in H_{max}/M_{max} ratio (partial eta squared = .29). The ICC values for normalized post-procedure response at the 10 s time point were .79, 70, .78, .73 and .76 from the five randomly generated data sets and .99 when generating the data sets by ascending or descending order of the normalized responses. A pattern of autocorrelation coefficients outside the "null" 95% confidence limits only occurred at 10 s post-procedure for lags ≤ 7, i.e., the occurrence of a non-random event. These autocorrelation coefficients at lags ≤ 7 that predominately measured correlations between *H/M* responses at 10 s post-procedure within groups were .56, .63, .55, .51, .45, .44, and .37, respectively and inferred a unique stimulus–response to each procedure. For all other time points and lags, autocorrelation coefficients were representative of the inherent variability of *H/M* responses, i.e., purely random events that were consistent across experimental groups. Five sequences of randomly re-assigned subject numbers (1–22) by group (1–3) revealed similar autocorrelation results. Ranges of autocorrelation coefficients at lags ≤ 7 at 10 s post-procedure from these randomly re-organized data sets were .60–.70, .53–.63, .50–.63, .47–.60, .44–.59, .46–.52, and .39–.47, respectively.

3.3. F-wave responses

The ICC values during the time series for F-wave amplitudes collected pre–post procedure by subject groups ranged from .81 to .95 with ICC values collapsed across all subjects being .94 and .90 pre and post procedures, respectively. There were no significant changes in F-response amplitudes among the groups and no events detected in the time series within any of the groups ($p > .05$). Fig. 4 summarizes the F-wave amplitude data that represented variations among subjects and between groups.

4. Discussion

Time series analyses of H_{max}/M_{max} ratios, pre–post a L5-S1 HVLA SM, substantiated the hypothesis that the specific aspects of the manipulative thrust lead to a greater attenuation of the H_{max}/M_{max} ratio as compared to the non-specific aspects related to the postural

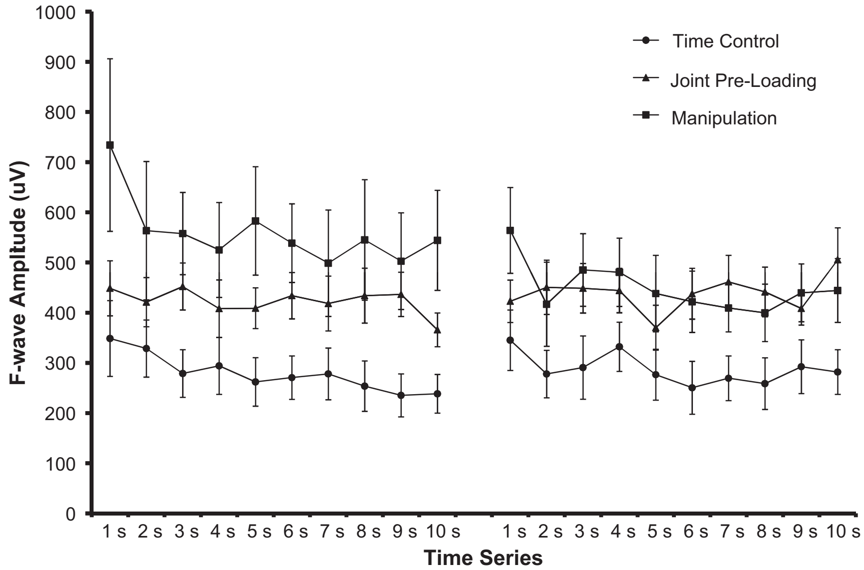

Fig. 4. Mean F-wave amplitudes (± SE) over time. F-wave amplitudes at 1-s intervals from 1 s to 10 s following either L5-S1 HVLA SM (■) or L5-S1 joint pre-loading procedure (▲) as compared to baseline values, pre-procedure. In the control condition (●) with subjects lying prone, F-wave amplitudes were recorded following a similar time course as for the experimental procedures.

perturbation and joint pre-loading. The attenuation of H_{max}/M_{max} ratio following the HVLA SM procedure was reliable. The time series analysis of the H_{max}/M_{max} ratio may hold promise as a translational tool to measure the consistency and accuracy of protocol implementation involving SMT in clinical trials research. As previously described in animal and human models (Avramov et al., 1992; Pickar, 1999, 2002; Kaufman et al., 2002; Dishman et al., 2005; Pickar et al., 2007), the discharge characteristics of Groups Ib, III, and IV afferents; muscle spindle aftereffects; and possibly the biostability properties of motoneurons are dependent on the types of manipulative thrusts and vertebral loading applied to the lumbar spine and may contribute to attenuation of the H_{max}/M_{max} ratio following a HVLA SM procedure. F-wave responses did not provide any new insights about central nervous function following a HVLA SM procedure.

Based upon data from asymptomatic subjects, it is difficult to compare the attenuation of the H_{max}/M_{max} ratio following HVLA SM reported in the current study and previously (Murphy et al., 1995; Dishman and Bulbulian, 2000, 2001; Dishman et al., 2002, 2005; Dishman and Burke, 2003) with the one dissenting report (Suter et al., 2005). The asymptomatic H-reflex data of (Suter et al., 2005), pre–post a sacroiliac joint manipulation using side-posture treatment and testing positions, were in contrast to previous H-reflex data reported by Murphy et al. (1995), in which the measurements of H-reflexes and sacroiliac joint manipulation occurred with asymptomatic subjects lying prone on a treatment table. The postural orientation for H-reflex measurements and joint manipulations may confound comparisons across research studies. A factorial experimental design comparing the various postural orientations for H-reflex measurements and joint manipulations is a necessary next step in the development of this potential translational tool.

When normalizing H-reflex amplitudes to a percentage of the control H-reflex amplitude, the proportion of motoneurons participating in the baseline test H-reflex, before the experimental procedure, may not be similar for all subjects and may confound the comparisons across experimental conditions, research studies and subject groups (Crone et al., 1990; Klimstra and Zehr, 2008). This potential confounder may explain why there were two distinct effects of HVLA SM on the magnitude of H-reflex amplitude in subjects with non-specific low back pain, which was attenuated for 60 s, as compared to asymptomatic subjects, no effect (Suter et al., 2005). What is interesting is that the reported attenuation of H-reflex amplitudes among the non-specific low back pain patients following HVLA SM is consistent with our concept of using H-reflex methodology as a translational tool to measure the consistency and accuracy of protocol implementation involving SMT in clinical trials research.

4.1. Technical delivery of the HVLA SM

In the current study, the critical factor differentiating the HVLA SM and joint pre-loading experimental conditions was the differences in the velocities of applying a load to the spine. Although articular crepitus is an empirical indicator of "successful" delivery of HVLA SM treatment, the relationship between the therapeutic benefit and articular crepitus (audible release or "cracking" "popping" sound) during HVLA SM lacks sufficient evidence to date (Ross et al., 2004; Evans and Breen, 2006; Herzog, 2010; Cramer et al., 2011). In addition, the location of the articular crepitus during side-posture lumbar HVLA SM is only generally accurate in identifying the spinal segment receiving the manipulative thrust (Ross et al., 2004). Reflex responses associated with HVLA SM treatments observed in asymptomatic subjects (Herzog et al., 1999) and the unique stimulus–response patterns of afferent discharges to manipulative-like thrusts in animal models (Bolton and Holland, 1998; Pickar, 1999, 2002; Sung et al., 2005; Bolton and Budgell, 2006; Pickar et al., 2007) provide support for our velocity dependent criterion. Reflex responses and altered afferent discharges are aligned with inhibitory mechanisms underlying HVLA SM (Pickar, 2002; Herzog, 2010). Articular crepitus is documented to occur during mobilization procedures, prethurst phase or preload application (Reggars, 1998; Herzog, 2010) and these procedures are not accompanied by reflex responses (Herzog, 2010). Conversely, reflex responses always occurred during HVLA SM treatments regardless of the presence or absence of articular crepitus (Herzog, 2010).

With respect to the technical delivery of the HVLA SM in the current study, the clinician had 20 years of experience as a practicing chiropractor. Articular crepitus was not a criterion for delivering the HVLA SM procedure. The clinician only applied a single

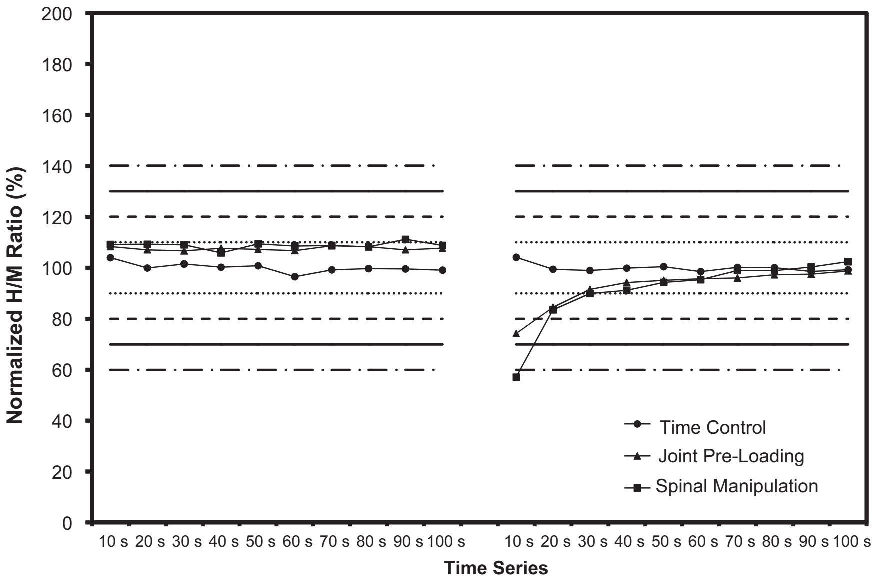

Fig. 5. The averaged time series for each of the experimental conditions using a subset of subjects that were matched on H_{max}/M_{max} ratios between 25% and 40%: time control (●, $n = 14$); L5-S1 joint pre-loading (▲, $n = 14$); and L5-S1 HVLA SM (■, $n = 14$). The subset data are comparable to Fig. 2, which shows the averaged time series for all subjects ($n = 66$, 22 per experimental condition). The subset data are also comparable to Fig. 1 in which immediate post-procedure at the 10 s time point, event detection, >3 SD, occurred in 10 of 14 subjects in the lumbar SM subset, in only 4 of 14 subjects in the joint loading subset and in none of subjects in time control subset ($\chi^2_{df=2} = 16.3$, $p < .05$).

thrust regardless of the presence or absence of articular crepitus. In three of the 22 subjects receiving the joint pre-loading procedure, the clinician noted the occurrence of articular crepitus. However, the inhibition of GM reflex was not detected in any of these three subjects. The data from the six subjects receiving the joint pre-loading procedure, in which inhibition of GM reflex was detected, supported the conclusion that some of the attenuation H_{max}/M_{max} ratio following HVLA SM was non-specific and dependent upon side-posture positioning and joint pre-loading. This conclusion agreed with previous research on: (1) the lack of relationship between articular crepitus and reflex responses associated with HVLA SM (Herzog, 2010); and (2) the non-specific effects of movement/position artifacts on H-reflexes following HVLA SM (Suter et al., 2005).

4.2. Limitations

The potential confounder of test reflex size on the susceptibility of the H-reflex to inhibition following HVLA SM requires further study. The use of H_{max} responses as the test size criterion was selected to enhance reliability of pre–post H-reflex measurements that occurred before and after experimental conditions involving a large postural perturbation. The test reflex size for the GM H-reflex that is most susceptible to inhibitory effects is between 25% and 40% of M_{max} (Crone et al., 1990). Although the distributions of the test reflex sizes (H_{max}) were similar among the subject groups, not all subjects had H_{max}/M_{max} ratios between 25% and 40%. However, Pearson's correlations for relative and absolute differences between H_{max}/M_{max} ratios at baseline and the 10 s post time point were low, $r =$ 12 and $r = .32$, respectively. In addition, applying the time series analysis to a subset of subjects matched on H_{max}/M_{max} ratios between 25% and 40% revealed similar results as summarized in Fig. 5. Larger submaximal M-waves on H-reflex trials recorded from the GM as opposed to the soleus muscle may be a confounder. Future studies may consider using the soleus H-reflex with the test reflex size set at 25% of M_{max} (Crone et al., 1990). GM H-reflex is measuring heteronymous conditioning effects of the L5-S1 HVLA SM procedure.

Although the attenuation of H_{max}/M_{max} ratio following the HVLA SM procedure was reliable, generalizability of time series analysis as it relates to the effectiveness of SMT still needs to be determined in a clinical setting. However in support our methodological approach, a time series of inherently variable motor evoked potentials (MEPs) following single-pulse or paired-pulse transcranial magnetic stimulations (TMS) during fatiguing contractions and immediately post-exercise, generate reliable experimental effects of inhibition or facilitation when averaged across multiple subjects from both healthy and patient populations (cf. Taylor and Gandevia, 2001; McNeil et al., 2009). Congruent with the time course of the effects of HVLA SM on the GM H-reflex, rapid residual decay of post-exercise facilitation of MEPs following contractions of different durations and intensities occurs within 10 s with a more gradual decay towards pre-exercise baseline values within 60 s (Balbi et al., 2002). Using a time series analysis of 20 MEPs recorded from the erector spinae following a single pulse TMS, the amount of post-procedure facilitation at the 10 s time point was unique to a L5-S1 HVLA SM as compared to joint pre-loading and time control (Dishman et al., 2008).

5. Conclusions

The time series analyses in the current research revealed that the attenuation of H_{max}/M_{max} ratio following a HVLA SM procedure was reliable and that some of the attenuation was non-specific and dependent upon side-posture positioning and joint pre-loading. The time series analysis of the H_{max}/M_{max} ratio may hold promise as a translational tool to measure the consistency and accuracy of protocol implementation involving SMT in clinical trials research.

Conflict of interest

None.

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