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The Neuromuscular Response to Spinal Manipulation: Quantifying the Effect of Pain with Electromyography

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Abstract

Objective

To establish a methodology to quantify the neuromuscular response to spinal manipulation, develop a comprehensive date set including factors that affect the response, and compare the responses in both healthy participants and participants with acute and chronic low back pain.

Methods

Surface and indwelling electromyography at eight muscle locations were recorded during lumbar side-lying manipulations in 20 asymptomatic participants, 20 acute pain participants, and 20 chronic pain participants. Onset delay detection was optimized for signal detection failures and methodological comparisons were performed using a generalized linear model. The number of muscle responses and muscle activity onset delays in relation to the manipulation contact force were compared across participant subclasses using mixed linear regressions. Effect sizes for all comparisons were calculated using Cohen's *d.*

Results

The method of muscle activity onset delay detection that best characterized the neuromuscular response to spinal manipulation was the double-threshold method with parameters of an 8 standard deviation amplitude threshold and a 10-msec duration threshold. In healthy participants, factors such as manipulation order and location had little effect on the neuromuscular response; however, the responding muscle location, layer and side revealed tendencies of lower response rates, and longer muscle activity onset delays as the distance from the manipulation location increased. Symptomatic participants had less muscle responses and longer muscle activity onset delays than the asymptomatic participants. Chronic pain participants had a greater tendency for shorter muscle activity onset delays than acute pain participants.

Conclusions

This study establishes a comprehensive database of both superficial lumbar and deep multifidus muscle activity and timing during spinal manipulation. The double-threshold method of muscle activity onset delay calculation is recommended over the cross-correlation method. Future studies in healthy participants focused on timing outcomes can be designed without regard for manipulation order and location within the parameters used in this study. Spinal manipulation may mediate pain through its influence on afferent activity of the muscle spindles and central nervous system. Participants in pain may experience more excitability in slower capsular reflex pathways than faster muscle spindle pathways compared to healthy participants, with the influence of the multifidi providing more pain-gating input to the central nervous system than superficial muscles. The neuromuscular response to spinal manipulation in participants in pain is dominated by the multifidus and is consistent with passive movements, as opposed to active movements that are dominated by superficial muscles.

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Stuart J. Currie

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CHAPTER 1: INTRODUCTION & OBJECTIVE

Low back pain (LBP) is a disabling medical condition with physical, psychological, and financial implications. There is no standard approach to the medical management of LBP, with treatment options ranging from pharmaceuticals, surgery, rehabilitation, manual therapies, daily activity modification, and rest. There is little information to indicate that any one of these treatment options is superior to the others. One reason for this is the complex nature of LBP, with pain generators including muscle, joint, bone, and disc. A more complete understanding of the mechanisms of these treatments will lead to a better ability to triage patients and match therapies with specific pathologies of the low back.

Spinal manipulation (SM) is a commonly used treatment for LBP typically performed by chiropractors, physical therapists and osteopaths. While this treatment is recommended for patients suffering from LBP, there are significant questions regarding its underlying mechanism. The goal of this dissertation is to develop a comprehensive data set of neuromuscular responses to SM in both healthy and LBP participants. This project is divided into four aims:

Aim #1: To establish appropriate analysis of neuromuscular response to SM by comparing two common methods (threshold detection and cross-correlation) of electromyography (EMG) muscle onset delay detection.

Aim #2: To identify treatment and response factors that affect the neuromuscular response to SM by systematically quantifying the muscle responses and muscle activity onset delays in healthy participants.

Aim #3: To determine the effect of the presence of LBP on the neuromuscular response to SM by comparing the muscle responses and muscle activity onset delays in healthy and LBP participants.

Aim #4: To investigate the connection of the neuromuscular response to SM to subclasses of LBP patients by comparing the muscle responses and muscle activity onset delays in participants experiencing chronic and acute LBP.

This dissertation is organized in the following manner. Chapter 2 provides general background that is applicable to all 4 aims. Included in this chapter is a review of the problem (LBP), an overview of spinal manipulation as applied to the problem, and a description of the anatomy relevant to the aims. Chapter 3 presents an overview of electromyography and its implications in the measurement of muscle onset detection as related to spinal manipulation. Chapter 4 is a methodological study, comparing two

methods for applying EMG onset detection to manipulation, with the goal of determining the best method to use in future investigations. Chapter 5 presents an overview of the measures and methods that have been used to quantify spinal manipulation and ends with a consideration of the treatment and response factors that affect the neuromuscular response to SM. Chapter 6 is a study that determines how treatment and response factors affect the neuromuscular response to SM in healthy participants. Chapter 7 identifies pain models that can be used to evaluate the response to SM, relates LBP to muscle function, and identifies subclasses of LBP. Chapter 8 is a study comparing the response to SM between healthy participants and those in pain to determine the effect of the presence of LBP the response to SM. Chapter 9 is a study comparing the neuromuscular response to SM in acute and chronic subclasses of LBP participants. Chapter 10 is a summary and conclusion. Appendix A contains the specific data processing methods used, background for the statistical methods, and an overview of the patient-centered questionnaires administered. Appendix B contains data in chart form for all 60 participants for comparison and reference. Appendix C contains anthropometric and questionnaire data for all participants. Appendix D is a summary of the conference presentations and publications that have resulted from this work.

CHAPTER 2: LOW BACK PAIN, SPINAL MANIPULATION AND SPINAL ANATOMY

2.1 Low Back Pain

Low back pain (LBP) is a common and disabling medical condition with physical, psychological, and economic implications. LBP is a significant public health problem that affects 80% of all adults in the United States at some point in their lives (Vallfors 1985). The prevalence of the US population experiencing back pain during any 3 month period is estimated at 17% (Deyo et al. 2006). In addition to its quality-of-life costs, it is financially damaging, with a median cost of $13,015 per quality-adjusted life year (Dagenais et al. 2008), and estimates that Americans spend $50 billion dollars per year on LBP (Andersson 1999). LBP is the fifth most common reason for all physician visits in the U.S. (Deyo et al. 2006). Even with its high expense, there is no uniformly accepted standard approach to medical care for LBP (Goertz et al. 2012). Drugs, surgery, rehabilitation, chiropractic, acupuncture, and massage are some of the forms of care used to treat this disorder.

There are many pain-generating anatomical structures in the area of the low back including numerous muscles, disks, vertebral facet joints, and nerves at each spinal level. The number of structures and the lack of reliable clinical tests to differentiate between

them, leads to difficulty in diagnosis and explains why "non-specific" LBP accounts for 85% of all LBP diagnoses (Deyo et al. 2006). Biomechanical explanations for LBP have been proposed and include, mechanical loading, functional pathology, and cell degeneration (Adams & Dolan 2005). The study of LBP relies on biomechanical concepts including force quantification, analysis of kinetics and kinematics, and mechanical property analysis to evaluate the mechanisms of therapeutic interventions.

2.2 Spinal Manipulation and Low Back Pain

A commonly accepted form of non-invasive care for LBP is spinal manipulation as performed by chiropractors, physical therapists, and osteopaths. SM has been practiced for thousands of years in several cultures (Hurwitz 2012) and is placed within the category of manual therapy techniques that are mechanical in nature involving force application to the spine to alleviate pain. In addition to SM, techniques that can be included in the definition of manual therapy include soft tissue mobilization, joint mobilization, muscle energy techniques, strain-counterstrain, and myofascial release techniques.

The federal government Agency for Health Care Policy and Research recommended that patients with LBP choose the most conservative care first, and found SM to be a safe and effective, drugless form of initial professional treatment for acute low back problems in adults (Bigos 1994). Spinal manipulation has been shown to be an effective treatment for acute LBP (Bronfort et al. 2004) and recently published clinical

practice guidelines have recommended it as an effective treatment (Chou et al. 2014). Evidence with regards to its efficacy over other common treatment is conflicting with SM showing greater improvements for pain and function than a placebo, but similar outcomes to other treatments such as medication and exercise (Michaleff et al. 2012); and a recent randomized trial found SM provided greater pain relief than usual medical care (Schneider et al. 2015). SM is recommended as an appropriate treatment for LBP, especially with acute LBP of less than 16 days duration (Childs et al. 2004); however, the published literature remains unclear on its effects in different patient populations.

Although SM is an accepted treatment for LBP, relatively little is known about the biomechanics of SM (Herzog 2010) leading to a call by the National Institutes of Health for research to determine if and how manual therapies alter biomechanics and activity in the human nervous system (Khalsa et al. 2006). The precise mechanisms by which SM alters musculoskeletal pain remain unclear, with current evidence suggesting an interaction between mechanical factors and the neurophysiological response (Bialosky et al. 2011; Pickar 2002). An evidenced-based model for the positive clinical effects of SM includes the following general mechanisms: mechanical stimulus, neurophysiological mechanisms, peripheral mechanisms, spinal mechanisms and supraspinal mechanisms (Je Bialosky et al. 2009). While more work is required to elucidate the underlying biomechanical mechanisms of SM, there has been progress in basic science quantification in several areas including anatomical research, manipulation forces, computational models, animal models, and the neurophysiologic response (Cramer et al. 2006).

Clinical prediction rules are tools used by clinicians to help decide when to use a particular treatment for specific conditions. However, because SM lacks a well-defined mechanism, attempts to develop prediction rules for SM (Childs et al. 2004) are necessarily limited in their scope. As more is learned about the structural and neuromuscular responses that occur during SM, these mechanisms will become clearer. As a result, clinicians will improve decision-making and more effectively pair specific treatment techniques with the appropriate patients and conditions.

2.3 Anatomy

The erector spinae (ES) muscles are the most prominent and superficial of all muscles posterior to the spine, traveling the length of the spine, while the multifidi (MF) are smaller, deeper muscles traveling 2-4 vertebral levels (Cramer & Darby 1995) (fig. 2.1). The MF originate from the spinous process and lamina of each lumbar vertebrae and descend in an inferior-lateral direction to insert several segments inferiorly (Macintosh & Bogduk 1986), while the ES describes a three-column group of muscles that travel parallel to the spine from the cervical to the lumbar region. Although the multifidus and erector spinae muscles are both extensors that contribute to lumbar spine stability, the action of the MF is posterior sagittal rotation of individual vertebrae while the lever arm of the ES may best contribute to broad motions (Macintosh & Bogduk 1986). The lumbar ES are innervated by the lateral branches of the dorsal rami of nearby spinal nerves, and the MF are innervated by the medial branches of the dorsal rami of nearby spinal nerves

(Cramer & Darby 1995). The forces of these intersegmental muscles are thought to play a role in spinal stiffness, stability and the control of intervertebral motion (Panjabi et al. 1989). The effect that SM has on the ES and MF are important to our understanding of the mechanisms of SM.

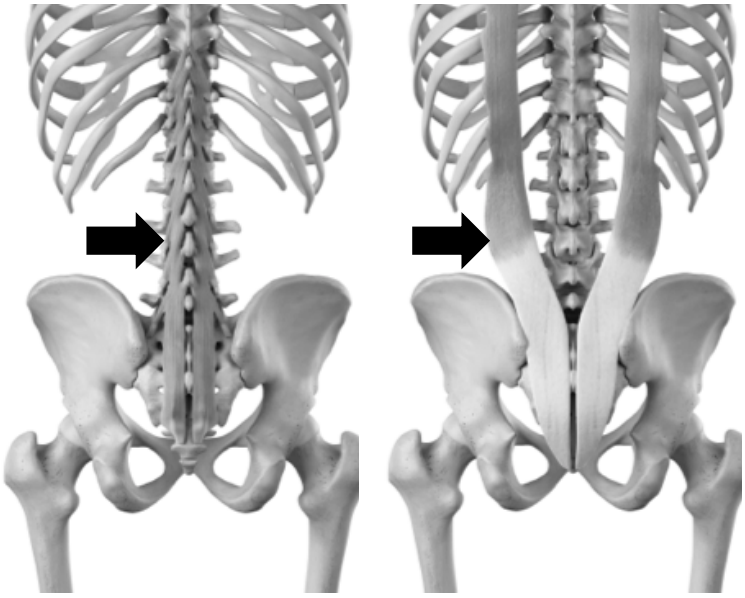

Figure 2.1. Posterior view of the human spine illustrating the deep multifidus muscle (left) and the superficial erector spinae muscle (right).

The spinal cord together with the brain forms the central nervous system. It is located in the spinal canal, travels the length of the spine, and is protected by the vertebral bodies. There are 31 pairs of spinal nerves, exiting at each vertebral level, that communicate afferent and efferent information to the neck, trunk and extremities . The spinal nerve consists of two roots within the intervertebral foramen. The dorsal root of each spinal nerve carries afferent sensory information including pain and proprioception from the periphery, while the ventral root conveys motor information to all muscles,

tissues and glands (Cramer & Darby 1995). The internal organization of the spinal cord, connecting afferent sensory information and efferent motor information, is visualized by a cross section of the spine. The butterfly-shaped or H-shaped gray matter within the spinal cord consists of a dorsal horn, a ventral horn and an intermediate region (fig. 2.2). A reflex arc consists of sensory information that is conveyed from muscles, tendons, joints and the vicera via spinal nerves to the dorsal horn of the spinal cord, synapses on interneurons within the intermediate region (where it may receive descending input from the brain), and then exits via the ventral horn to synapse with motor neurons to cause a response (Cramer & Darby 1995).

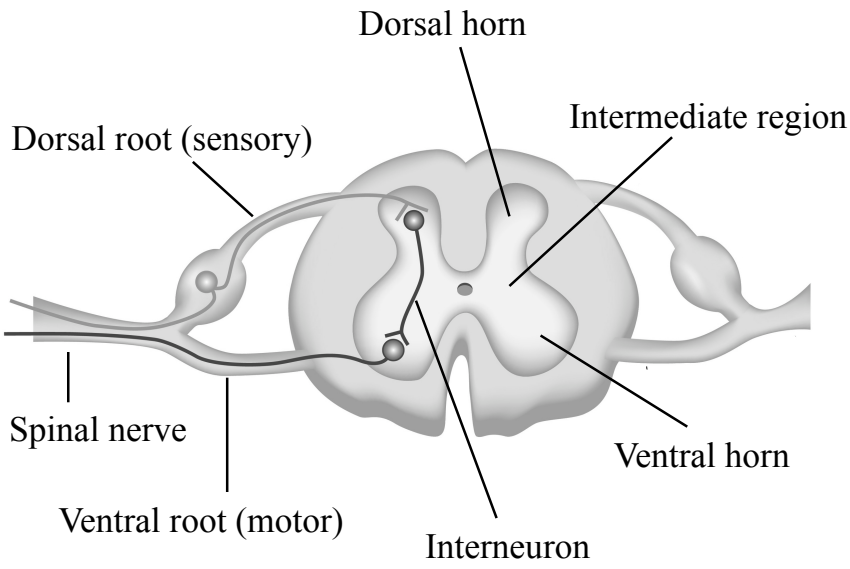

Figure 2.2. Cross-section of the spinal cord illustrating the spinal nerves. Sensory information from the periphery travels through the dorsal root to the dorsal horn of the spinal cord, synapsing on interneurons in the H-shaped gray matter to connect to motor nerves which exit via the ventral horn traveling through the ventral root back to the periphery.

CHAPTER 3: ELECTROMYOGRAPHY AND SPINAL MANIPULATION

3.1 Electromyography

3.1.1 Electromyography Overview

Kinesiologic EMG is a method of analyzing muscle function during human movement that has evolved significantly over the last 50 years. EMG detects the electrical potential generated by the functional unit of the neuromuscular system – the motor unit – and in its most basic form is used to evaluate muscle activity, function and fatigue. The myoelectric signal recorded at the surface of the skin is the summation of all the motor unit action potentials in the area of the electrodes (G. Soderberg & Knutson 2000). EMG is a tool that can be used to assess muscle function as a result of a therapeutic procedure, provide biofeedback, assess muscle onset time, asses gait, and analyze muscle strength.

There are several methodological issues to consider when analyzing the results of kinesiologic EMG studies. Instrumentation, electrical noise, mechanical and stimulus artifacts, and cross-talk must be considered in order to obtain accurate results (Kamen & Gabriel 2010). In addition to processing considerations, post-collection decisions including filtering and post-processing of EMG data can affect how the data is interpreted. In general terms, filtering is done in order to eliminate unwanted signal

(noise) while preserving the frequencies of interest. Filtering decisions affect the quality of data and must be justified with sound logical reasons. Equipment noise generated by the recording amplifier, electrical noise (50-60Hz), movement artifacts (<30Hz), and differences between surface (20-500Hz) and indwelling (>500Hz) recordings must be considered (Türker 1993).

3.1.2 Electromyography – Amplitude and Timing

Quantifying EMG data can take several forms, with muscle activity amplitude and timing (muscle "on" or "off") being two of the most common applications. Both amplitude and timing measures have significant clinical value, with each having its respective advantages and disadvantages. The interpretation of amplitude measures between subjects and even within subjects on different days can be problematic, requiring a normalization of the data to a maximal voluntary contraction (G. Soderberg & Knutson 2000). This can be problematic as the ability to maximally activate all motor units for this process depends on many variable factors, such as the muscle activated, training level and motivation level of the participant. Some authors have questioned the validity of normalized data as it may alter a statistical feature, the coefficient of variation, when compared to non-normalized data (Allison et al. 1993). The evaluation of timing parameters using EMG is commonly used in human movement and kinesiological research. Muscle activity onset as detected by EMG is of high clinical interest; however, little agreement exists as to a standard method to measure this parameter (Hodges & Bui 1996). Because the difference from stimulus to the onset of muscle activity may be on the

order of several milliseconds, the accuracy of onset determination is critical in movement studies.

Recent improvements in algorithms used in the temporal analysis of muscle activation have allowed activation onset to be more accurately and robustly determined. One such method, the Teager-Kaiser energy operator (TKEO) has been shown to significantly improve the accuracy of threshold-based onset detection methods (Li et al. 2007). The TKEO operator is defined in the time domain as:

$$\Psi[x(n)] = x^2(n) - x(n+1)x(n-1) \qquad 3.1$$

Where n is the sequence index, and x is the amplitude of the signal. The purpose of the TKEO is to better visualize the onset of muscle activity by simultaneously detecting the instantaneous changes in the frequency and amplitude allowing easier and more accurate onset detection (fig. 3.1). The addition of this conditioning method may improve the accuracy of threshold-based onset detection methods, regardless of the signal to noise ratio (Solnik et al. 2008).

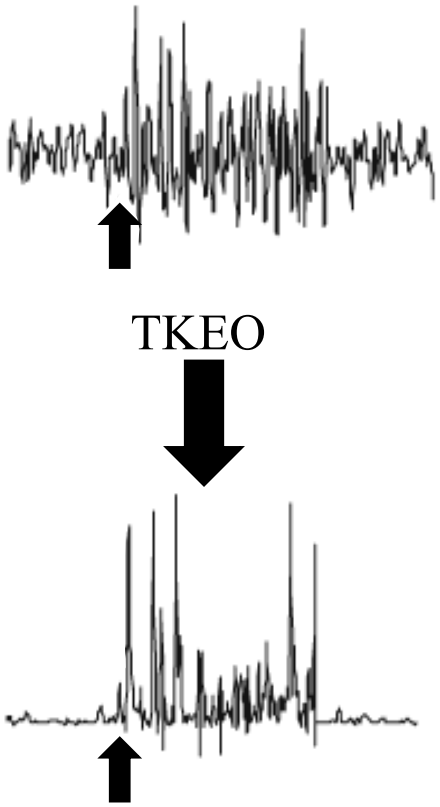

Figure 3.1 An example of a raw EMG signal (top) and its corresponding signal after TKEO transformation. The short arrows indicate onset time of muscle activity. *Source*: Data adapted from Li 2007, figure 1.

3.1.3 Instrument Considerations

Subsequent to a determination of the muscles of interest, the type of EMG instrumentation must be chosen. One of the first considerations in this regard is whether to use skin mounted surface electrodes, or indwelling fine-wire electrodes. Surface electrodes can be active or passive and are placed on the surface of the skin in order to infer the electrical activity of the subcutaneous muscles. The passive surface electrodes most commonly used in kinesiologic research do not have a high input resistance and are therefore affected by changes in skin resistance (Türker 1993). The skin surface must be

cleaned of dead cells, removed of oils using alcohol and abraded in order to reduce the presence of nonconductive elements between the electrode and the element itself. Surface electrodes have the limitation of tending to record simultaneous muscle activity from adjacent muscles (Stokes et al. 2003). Indwelling electrodes are wire-based and inserted by needle to record the activity of small muscles deep within the body. While complications such as muscle damage and wire fracture are extremely low (Jonsson & Bagge 1968), patient discomfort can be an issue (Jonsson et al. 1968). Indwelling electrodes, while offering the advantage of being able to reach muscles that are not accessible by surface electrodes, necessarily come with the complication of uncertainty of the location of the electrode. Verification of the electrode location by techniques such as stimulation, muscle testing or ultrasound is strongly recommended (G. Soderberg & Knutson 2000)

3.1.4 Onset Detection – Threshold Method

There are a wide variety of techniques used to determine the onset of EMG muscle activity. Common characteristics among the techniques involve a determination of the earliest increase in EMG activity above some predetermined steady state or baseline, known as the threshold method. The threshold selected to make this onset detection is often arbitrary and significantly affects the results and interpretation (G. Soderberg & Knutson 2000). Consideration for how the EMG data is filtered and smoothed using the root mean square operation or a linear envelope is necessary prior to threshold detection. EMG data can displayed within an interactive graphical software to

enable the investigator to determine the onset to the nearest millisecond (Hodges & Bui 1996). Visual determination has been compared to computer determination and found to vary significantly. Careful selection of methods is advocated, given that errors of up to 167% of reaction time have been reported (Hodges & Bui 1996). Although the determination of whether a muscle is "on" or "off" by this method necessarily involves a subjective component, this visual inspection can also lead to discoveries about the data in question such as background noise and artifacts, and can help identify idiosyncrasies specific to the data set.

3.1.5 Onset Detection – Cross-correlation Method

The difficulty in processing large amounts of human movement data has led to a constant search for more powerful and efficient tools. Cross-correlation analysis is based on the Pearson product moment correlation used in statistical analysis, with the distinction that the cross-correlation method uses time varying signals instead of discrete points from multiple participants or samples (Nelson-Wong et al. 2009). The process of cross-correlation involves holding one signal steady while a second signal is time shifted forwards and backwards over the entire length of the record. Correlation can be calculated at each time shift to create a cross-correlation function and thus, the value of the time shift can be considered the phase lag between the two signals. The equation for the cross-correlation coefficient is:

$$R_{xy}(\tau) = \frac{1}{T}\frac{\int_0^T x(t)y(t \pm \tau)\mathrm{dt}}{\sqrt{R_{xx}(0)R_{yy}(0)}} \qquad 3.2$$

Where T is the duration of the record, the numerator is the integration of the products of the two signals at each point, where $x(t)$ is held stationary and $y(t)$ is phase shifted by τ. The autocorrelations are multiplied together in the denominator to remove the units and produce a dimensionless number between -1 and 1.

Cross-correlation can be used to determine spatial and temporal congruency and similarities between two time varying signals. It is especially useful in pattern recognition within a signal or temporal similarity between two signals. One of the most powerful output measures is the temporal shift (τ) of one signal relative to another. The value of τ has been used in studies determining muscle onset latencies, order of muscle recruitment and can be used to evaluate the relation of muscle function to a mechanical event (Nelson-Wong et al. 2009). Another major advantage of cross-correlation is that two signals being compared are not required to have the same units; they are however, required to have the same record duration and an equal number of data points. This presents challenges with regards to two signals that are sampled at different frequencies, and requires downsampling or interpolation. In addition, cross-correlation method is subject to inaccuracies when the signal to noise ratio is low.

3.2 Electromyography and Spinal Manipulation

Spinal manipulation may affect the function of the nervous system by correcting anatomical, physiological or biomechanical dynamics of the vertebrae (Pickar 2002). Theories regarding these mechanical influences include that SM relieves vertebral compression of spinal nerve roots (nerve compression theory), SM relieves aberrant

stimulation to neural reflex centers (reflex theory) and SM causes hypoalgesia through central facilitation of the spinal cord (pain relief theory); with sufficient evidence to develop working models but insufficient evidence to consider any one of them alone valid (Haldeman 2000). While the study of altered nervous system activity is limited in humans, altered muscle activity during SM has been shown in animal models with changes in muscle spindle firing demonstrated in feline specimens with various spinal manipulation parameters (Pickar & Kang 2006). Animal models provide a foundation on which to confirm or deny hypotheses of altered activation in humans.

The primary tool used to infer information about the neuromuscular effect of spinal manipulation is EMG. Surface EMG involves the recording of myoelectric signals from the surface of the skin, giving insight into the neuromuscular response to manipulation. While direct measurement of afferent activity during a clinical treatment is difficult, the efferent signal as measured by EMG is a surrogate measure for afferent input to the spinal cord from muscle spindles (Vallbo 1970; Dimitriou 2014). Early work in the area of electromyographic responses to spinal manipulative therapy included the quantification of the activity of back muscles in the thoracic spine, revealing a reflex response to SM (Herzog, P. Conway, et al. 1995). Characteristics of the activity indicated it was likely a muscle spindle reflex (Herzog, P. Conway, et al. 1995) which was not restricted to the site of the treatment application (Herzog et al. 1999). It was also shown that when a manipulation impulse was applied, EMG activity was abolished in some patients indicating a relaxation phenomenon (Herzog 2000). It was not determined why this reflex response occurred in some participants and not others. It was concluded that

SMT elicited a reflex response that was not necessarily localized and may affect regions that are distant from the treatment site (Herzog 2010).

The EMG amplitude measurements recorded in spinal manipulation studies have not always produced consistent results (Lehman 2012). Some have found reductions in resting EMG activity (DeVocht et al. 2005), some have noted an excitatory effect (Dunning & Rushton 2009) and others have found no significant change (Lehman & McGill 2001). While many studies have focused on static muscular function, others have evaluated dynamic tasks following manipulation. The importance of evaluating the muscular response during a variety of activities is seen in the results of a study evaluating the response to a side posture SM during flexion and extension tasks. No change in muscle activity was seen during the dynamic flexion phase, but a significant decrease was seen during the full forward flexion phase and the extension phase (Bicalho et al. 2010). Spinal manipulation appears to be associated with short term changes in the amplitude of the EMG signal, and larger studies conclude that when a change is present in the paraspinal muscles, it is a reduction in amplitude (Lehman 2012).

Manipulation impulses using both mechanical and manual methods have resulted in significant timing differences in parapsinal EMG activity (Colloca & Keller 2001; Lehman & McGill 2001). These differences are not consistent however, with several review articles documenting the variable EMG response to manipulation including both inhibitory and excitatory results (Lehman 2012; Cramer et al. 2006). Using needle EMG a temporal delay in multifidus onset of 2-18 milliseconds has been observed following SM (Colloca et al. 2003). A positive reflex response was defined as a response that was at

least 5% of the average peak isometric extension response. There is no discussion as to the rationale for choosing this threshold for activity. A review article notes this is "surprisingly fast" for a reflex response (Cramer et al. 2006). Temporal delays of 50-400ms in the paraspinal muscles as measured by surface EMG have been observed, with variability depending on differences in the application of the manipulation impulse (Herzog et al. 1999). The reflex activity following SM has been observed throughout a 273 msec measurement interval, found to reach its peak within 50-100 msec and been initiated by the pre-load phase of the posterior to anterior thrust application (Colloca & Keller 2001).

In addition to neuromuscular implications, the biomechanical changes caused by SM are thought to have physiological consequences by means of affecting the flow of sensory information to the central nervous system. Transcranial magnetic stimulation (TMS) measures the physiology of the nervous system between the brain and muscle by creating an evoked potential that is measured at the targeted muscle. Using TMS it was determined that SM applied to the lumbosacral joint produced a significant decrease in corticospinal and spinal reflex excitability, while no significant change occurred after the control intervention (Fryer & Pearce 2012). This provides evidence for the central nervous system's role in the mechanism of spinal manipulation.

Significant variability exists in the methodology used to record the characteristics of the neuromuscular response making comparison across studies difficult. There is no standard method to record amplitude or timing measures for use in the study of SM. Given that visual onset determination is subjective and inaccuracies have been reported in

the 5-20 ms range (Hodges & Bui 1996), the importance of a standard for methods and reporting in the comparison across subjects and studies is magnified. Like much of the kinesiological research, the study of manipulation is complicated by the moving parts – both participant and clinician - as well as instrumentation hurdles, and will only be improved through the introduction of protocol and processing standards.

CHAPTER 4: METHODS OF MUSCLE ACTIVATION ONSET TIMING DURING SPINAL MANIPULATION

4.1 Introduction

Spinal manipulation is a treatment used by doctors of chiropractic, doctors of osteopathy, and physical therapists to address a wide variety of musculoskeletal conditions (Meeker & Haldeman 2002). Although high-velocity low-amplitude (HVLA) spinal manipulation is a recognized treatment for acute and chronic low back pain (Bigos 1994), questions about the underlying biomechanical mechanisms of effective treatment remain unanswered. For example, the ideal amount of relative vertebral movement, the importance of a muscular reflex response, and the role of joint cavitation (audible release) all remain unclear (Herzog 2010). By developing a better understanding of how these aspects contribute to pain relief through in-vivo research, improvements can be made in the pairing of specific treatments with patient and clinical condition.

In-vivo research on SM has largely focused on mechanical parameters such as external contact force, vertebral movement, and cavitation, while few investigations have examined the neuromuscular response to the manipulation itself. This response consists of integrated communication between the sensory system (i.e. mechanoreceptors) and the motor system (i.e. muscles). Sensory system responses to SM include positive action potentials in spinal nerve roots (Colloca et al. 2003), increases in central nervous system

excitability (Dishman et al. 2002), and decreased sensitivity to pain (Terrett & Vernon 1984). The motor system response to SM includes both increased and decreased paraspinal muscle EMG activity [Herzog et. al., 1999; Herzog et al., 1995; DeVocht et al., 2005]. Mechanisms that may explain these effects are altered inflow of proprioceptive primary afferents (group I and II) from the paraspinal tissues, mechanical compression of neural tissue, central nervous system sensitization, and altered motorneuron excitability (Pickar 2002).

Two characteristics of the EMG response to SM are relevant for examination: *amplitude of the response* and *timing of the response*. Evidence of EMG amplitude changes following SM is conflicting (Lehman & McGill 2001; Lehman 2012), which creates difficulty when interpreting the meaning and significance of amplitude changes in response to SM. A recent review of EMG and SM indicated that manipulation is associated with short-term changes in the amplitude response of the myoelectric signal, but that the response can be either an amplitude *increase or a decrease*, and may be specific to the proximity of the muscle to the force application and activity performed (Lehman 2012). In addition, interpretation of the amplitude response across participants can be difficult as it is dependent on the type of muscle studied, the training level, and participant motivation.

Timing of the muscle response is quantified as the muscle activity onset following the application of the contact force. Pickar et al. (Pickar & Kang 2006) demonstrated that the frequency of muscle spindle firing increases in response to forces consistent with SM, which may incite timing changes in efferent motorneuron activity. The muscle activity

onset delay measured after a manual posterior to anterior SM in the thoracic spine was 50-200 msec, a range that suggests a muscle spindle pathway reflex (Herzog, P. Conway, et al. 1995). In contrast, the muscle activity onset delay measured after a SM performed with a mechanical device applied directly to L1 and L3 spinal vertebra in a posterior to anterior direction was 2.4-18.1 msec (Colloca et al. 2003).

Two common methods are available to calculate the muscle activity onset delay: double-threshold detection and cross-correlation. It is currently unclear which method is most appropriate for calculating onset delays in response to SM. Considering the wide range of onset delays reported in the literature (≈ 2-200 ms), and that forces are applied by practitioners in variable settings, there is a need to facilitate comparison between investigations by standardizing methodologies. The double-threshold method, which is more commonly used, requires identification of an amplitude threshold and a duration threshold over which EMG activity is considered muscle "active" (Hodges & Bui 1996). The cross-correlation method uses the cross-correlation function to identify the temporal shift (or time lag) between 2 time-varying signals, and has been used in human movement and rehabilitation sciences to evaluate muscle activity (Nelson-Wong et al. 2009).

Specific details of how muscle activity onset delays are calculated within each investigation are sometimes sparse, and a comparison of methodologies does not exist. Therefore, the objectives of this investigation were: 1) To determine the threshold parameters that most reliably characterizes the muscular response to SM using the double-threshold method of EMG onset detection, and 2) To evaluate the advantages and

disadvantages of the double-threshold method and cross-correlation methods when applied to HVLA spinal manipulations in healthy participants. This information will help develop methodological standards on which to compare the EMG responses in research on SM and assist interpretation and applications of EMG in research and clinical practice.

4.2 Methods

4.2.1 Participant information

Seventeen participants with no history of low back pain during the previous 4 years (table 4.1) visited the laboratory for 1 session lasting 3 hours in which lumbar muscle activity was collected during SM. Each participant was screened for contraindications to SM by performing an orthopedic and neurologic examination. Participants were excluded from the investigation if: their current level of pain exceeded a 7 out of 10 on a verbal pain scale; they experienced radicular pain below the knee during orthopedic testing; or neurologic exam revealed absent reflexes, decreased sensation or weakness below the knee. Each participant provided written, informed consent in accordance with the Colorado Multiple Institutional Review Board prior to the start of the experimental session.

Table 4.1. Mean ± SD participant anthropometric information.

	Male (n=9)	**Female (n=8)**
Age (years)	31.6 ± 13.4	28.8 ± 5.2
Height (cm)	179.4 ± 7.7	165.0 ± 3.3
Weight (kg)	79.9 ± 6.4	59.0 ± 4.7
Dominant Hand (right/left)	(8/1)	(6/2)

4.2.2 Application of spinal manipulation

Two doctors of chiropractic, each with over 10 years of clinical experience, performed HVLA SM at the L3 and Sacroiliac (SI) spinal level with a hypothenar contact in the side-lying position. The order of manipulations was randomized, the time between manipulations was between 1 and 3 minutes, and only data from the manipulation at L3 were used in this analysis.

4.2.3 EMG and contact force instrumentation

Each participant was instrumented with surface EMG over the left ES at the L2 level and indwelling EMG (50mm, 25ga needle with a pair of 0.051mm, insulated, hooked wires and 200mm tail with 5mm bare-wire terminations) in the left MF at the L2 spinal level (fig. 4.1) according to a previously defined insertion protocol(Haig et al. 1991). These recording sites were a subset from a larger protocol in which multiple levels of the lumbar multifidi and ES were similarly instrumented (fig. 4.1). Recordings at L2 were chosen to analyze in this investigation for their close proximity to the site of manipulation (L3). A Noraxon TeleMyo DTS (Noraxon USA, Scottsdale AZ) system was used to record both surface and indwelling EMG signals. The force from the practitioner's contact hand was estimated using an optimized algorithm that combines measurements from a force plate (Bertec Corporation, Columbus, OH) embedded in the treatment table and force transducers attached to the practitioner while maintaining natural contact between the practitioner and the participant (C. Myers et al. 2012) (see appendix A.2 for a full description of the optimization methods).

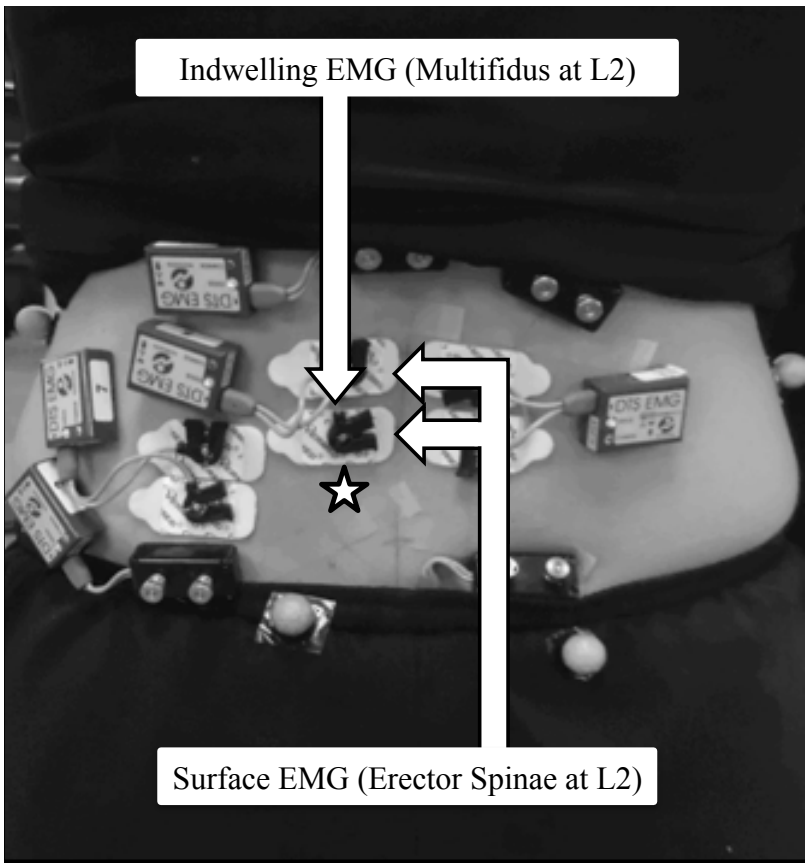

Figure 4.1. Instrumentation of indwelling and surface EMG. The indwelling EMG recorded information from the multifidus and the surface EMG from the erector spinae. Star indicates manipulation site at the L3 spinal level on the left.

4.2.4 Electromyography signal processing

The raw EMG signals were sampled at 2000 Hz, bandpass filtered to remove movement artifact and high frequency noise (4th order Butterworth, 15-350Hz), and transformed using the TKEO (Li et al. 2007; Solnik et al. 2008) (equation 3.1). Following TKEO transformation, linear envelopes of the ES and MF EMG signals were created by applying full-wave rectification and low-pass filter (4^{th}-order Butterworth, 50Hz cutoff).

4.2.5 Onset delay calculations

Onset delay between the contact force and muscle activation was calculated using the double-threshold method (Kamen & Gabriel 2010) with varying threshold parameters, and the cross-correlation method (Nelson-Wong et al. 2009).

4.2.6 Onset delay using double-threshold method

Muscle activation onset was determined using 3 different amplitude thresholds and 3 different duration thresholds (9 combinations total). The amplitude thresholds were 3, 8, and 13 standard deviations (SD) above mean baseline amplitude recorded 1 second prior to manipulation. The duration thresholds chosen were 0, 10, and 20 msec. The muscle was considered "active" if the signal passed the amplitude threshold for the given duration threshold. The onset of contact force application was determined by the initiation of positive rate of force. Muscle activity onset delay was recorded as the difference between these times (Figure 4.2A) (see appendix A.4 for a full description of muscle activity onset delay calculations).

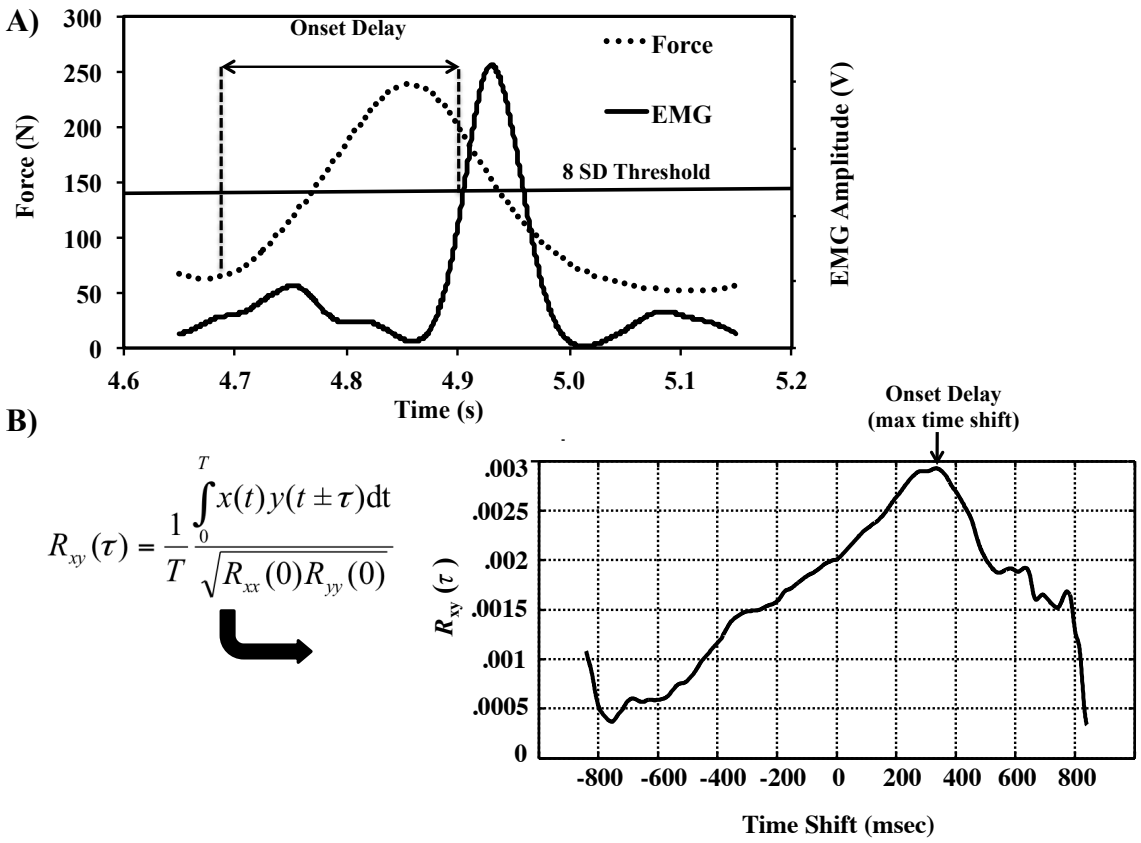

Figure 4.2. Illustration of two methods used to determine EMG onset delay. A) Onset delay as calculated by the double-threshold method using the difference between the onset of positive force rate and muscle activity that crossed the threshold. B) Onset delay as calculated using the cross-correlation function lag plot. The time at which the maximum value occurs represents the time shift between the two signals.

4.2.7 Onset delay using cross-correlation method

The cross-correlation function (equation 3.2) between the contact force and EMG linear envelope was evaluated using the *xcorr* function in Matlab (The MathWorks Inc, Natick, MA). Muscle activity onset delay was defined as the time shift that corresponded with the maximum value of the cross-correlation function lag plot (Figure 4.2B).

4.2.8 Selection of thresholds and comparison to cross-correlation method

The combination of amplitude threshold and duration threshold that minimized 2 error variables (number of signal dropouts, number of false positives) was chosen for comparing the muscle activity onset delays to those calculated by the cross-correlation method. A signal dropout in the double-threshold method was defined as any instance in which the EMG activity did not meet both thresholds. A false positive in the double-threshold method was defined as EMG activity that crossed the threshold but was not visually different from baseline (fig. 4.3). The collective effect of the dropout rates and false positives was considered the total detection failures. To choose the parameter combination, we emphasized minimizing false positives over minimizing dropouts.

$$Detection\ Failures = Signal\ Dropouts + False\ Positives \quad (4.1)$$

The onset delays calculated using the previously chosen double-threshold parameters were compared for both muscle groups to the onset delays calculated using the cross-correlation method using a generalized linear model. Level of significance of all comparisons was set at $\alpha=0.05$. All statistical analyses were conducted using MINITAB (version 16.0) and Microsoft Excel.

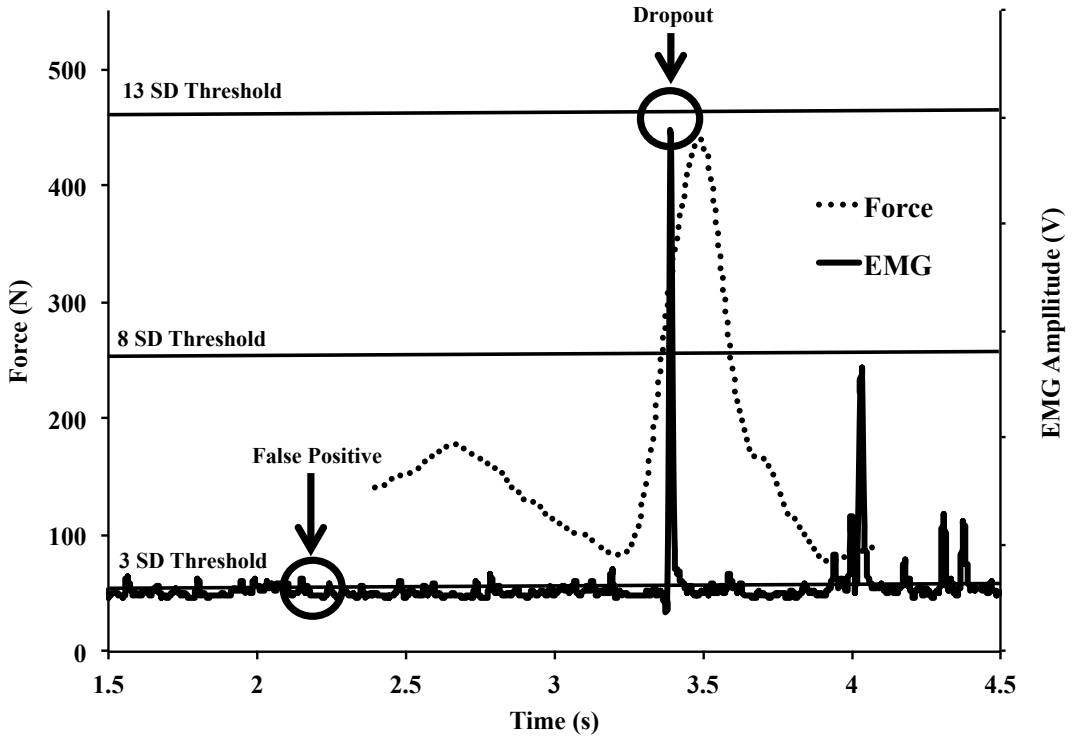

Figure 4.3. Illustration of the two errors (false positives and dropouts) in onset delay calculation using the double-threshold method. A false positive occurred when EMG activity crossed the threshold but was not different from baseline and a dropout occurred when the activity did not meet the threshold criteria.

4.3 Results

4.3.1 Contact force during spinal manipulation

The mean peak contact force applied by the hand of the practitioner during the manipulations was 529.5±152.4 N and ranged from 242.2 to 940.2 N. The time between onset of contact force application and peak force was 243±80 msec.

4.3.2 Double-threshold parameter selection

Higher amplitude thresholds and higher duration thresholds both corresponded with higher muscle activity onset delays (table 4.2). The two parameter combinations of amplitude and duration thresholds that resulted in the lowest *Detection Failures* were the '8SD-0msec' (*Detection Failures* = 8) and the '8SD-10msec' (*Detection Failures* = 9) combinations (fig. 4.4).

Table 4.2. Mean [95% CI] onset delays (msec) for nine combinations of double-threshold parameters for both multifidus and erector spinae. Negative values indicate EMG activity that occurred prior to the onset of positive force rate. Parameters with the lowest *Detection Failures* are boxed.

		Multifidus			**Erector Spinae**		
Duration Thresholds (msec)		**0**	**10**	**20**	**0**	**10**	**20**
Amplitude Thresholds (SD)	3	19 [-743, 781]	13 [-145,171]	127 [13,242]	-100 [-1301, 1100]	-99 [-334, 136]	218 [120, 316]
	8	**137 [73, 202]**	**149 [65, 233]**	171 [85, 258]	**185 [80, 289]**	**252 [106, 397]**	252 [106, 397]
	13	164 [77,251]	188 [101, 275]	193 [91, 294]	304 [79, 530]	365 [149, 600]	292[129, 455]

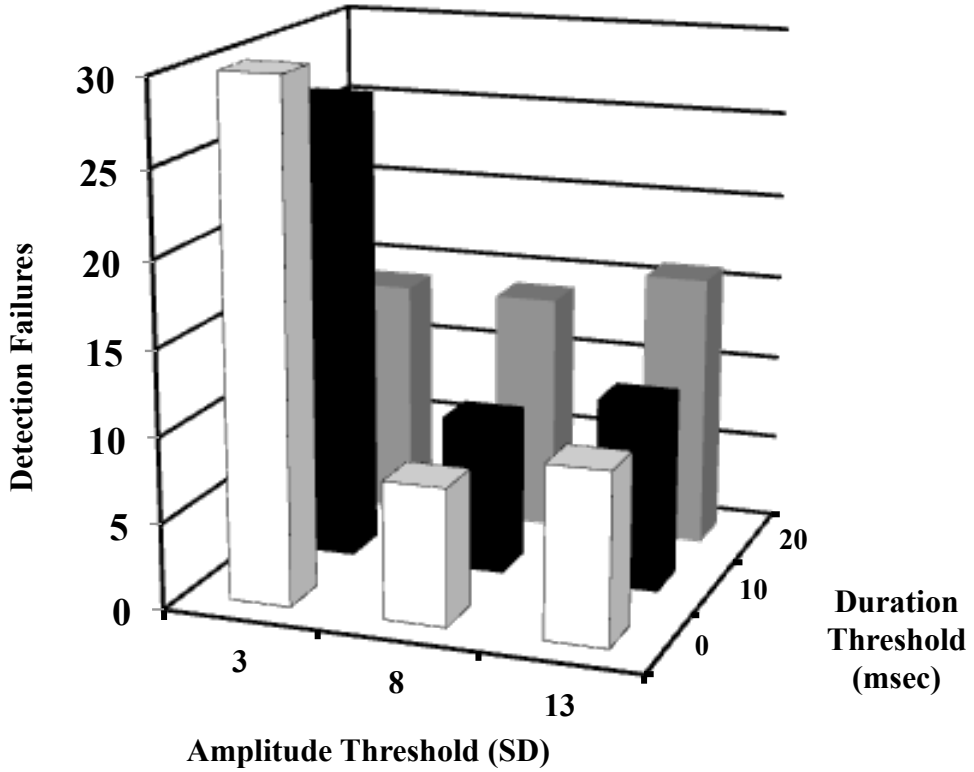

Figure 4.4**.** Plot of the *Detection Failures* for the amplitude threshold (3, 8, and 13 standard deviations) and the duration threshold criteria (0, 10, and 20 msec). The number of *Dectection Failures* is the sum of the number of dropouts and the number of false positives. The lowest values represent the best minimization of false positives and dropouts. The total number of observations was 34 (17 MF onset delays and 17 erector spinae onset delays).

We chose the '8SD-10msec' threshold combination for comparison to the cross-correlation method. The '8SD-10msec' parameter combination was chosen because it resulted in 0 false positives compared to 6 false positives for the '8SD-0msec' combination.

4.*3.3 Comparison between methods and muscles*

The mean EMG muscle activity onset delay for the '8SD-10msec' double-threshold method across participants was 149±152 msec and 252±204 msec for the MF and ES, respectively. The EMG onset delay for the cross-correlation method was 26±101 for the MF and 67±116 for the ES (Figure 4.5).

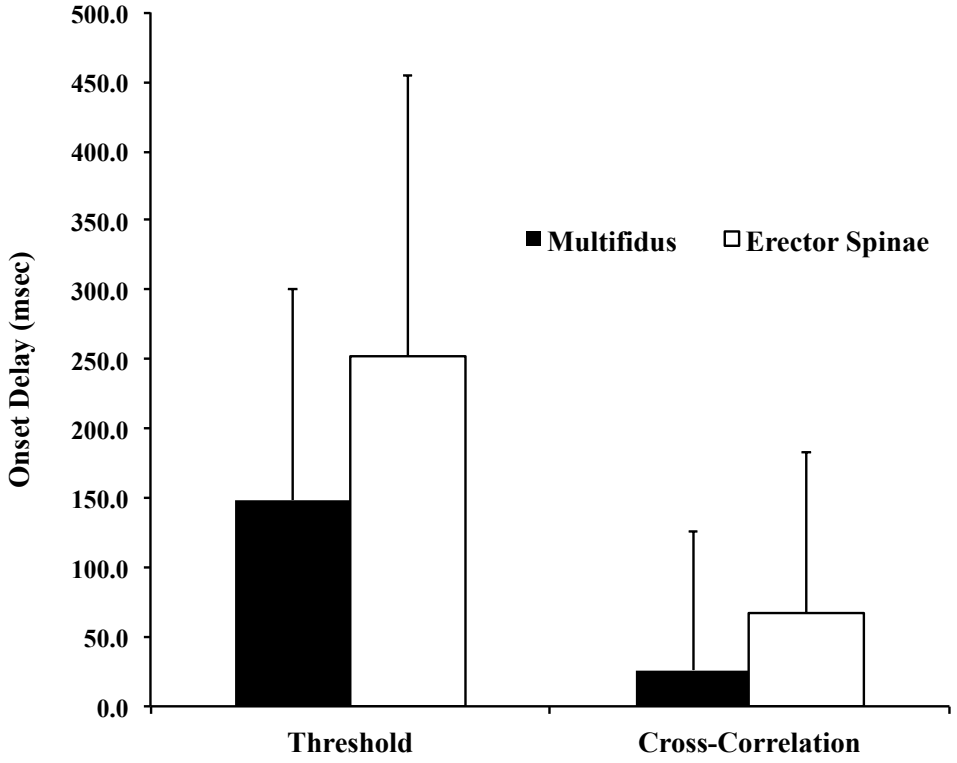

Figure 4.5. Mean ± SD muscle activity onset delays for multifidus and erector spinae are compared using the double-threshold method and the cross correlation method.

There was no interaction between muscle and method (F=0.61, p=0.44). There was no main effect for muscle (F=3.28, p=0.08); but there was a main effect for method (F=14.88, p=0.00). There were no statistical difference between the 2 muscle groups (T-Value = -1.41, p=0.166), however a trend of smaller onset delays across methods in the

MF (85±140) compared to onset delays in the ES (151±183) was noted. Onset delays were significantly different for the double-threshold method and the cross-correlation method (T-Value = 3.57, p=0.001).

4.4 Discussion

This investigation is the first to quantify MF and ES muscle activity during a side-lying spinal manipulation with the goal of developing a common method to detect muscle activity onset delay. We chose the 8 SD amplitude threshold and the 10 msec duration threshold as the combination that most accurately and reliably detected onset delay in response to SM. Onset delays using cross-correlation were also calculated, and compared to the double-threshold method. The large differences between methods and threshold parameters illustrate the importance of accurately reporting timing methods. The cross-correlation method has advantages in processing time and simplicity requiring less supervision, but introduced complexities when interpreting onset delays in some signals. The double-threshold method had the advantage of confirming the relation of muscle activity to contact force during supervision, but required more processing time and was subject to more human influence.

For the double-threshold method, we chose the combination of 8 SD for the amplitude threshold and 10 msec for the duration threshold as parameters that allowed confident calculation of muscle activity onset delays. These parameters minimized both the dropouts and false positives and allowed identification of activity with confidence

that it was not baseline activity or noise. The duration threshold of 10 msec corresponds with previous work that identified 25 samples (sampled at 1000 Hz) as a good parameter when EMG data are transformed using the Teager-Kaiser Energy Operator (Solnik et al. 2008). We also considered the '8SD-0' msec parameter combination, but it would have resulted in a large number of false positives. Little consensus exists for the threshold criteria for determining EMG onset, and visual inspection remains the standard against which new algorithms are tested (Hodges & Bui 1996).

A change in amplitude threshold or duration threshold systematically changes the number of *Dectection Failures* as a result of increasing *False Positives* or *Dropouts*. Changing the amplitude threshold from 8 SD to 3 SD increases the number of *False Positives* and changing the standard deviation from 8 SD to 13 SD increased the number of a *Dropouts*. By eliminating the duration threshold ('8SD – 0msec'), muscle activation onset was identified when the threshold criterion was met; however, they occurred far in advance of the contact force and were not discernable from baseline activity in some cases (Figure 3). *False Positives* are highest for the 3 SD amplitude parameter; therefore, inclusion of these data as true muscle activation would result in inaccurate onset delay. The importance of visualizing all data before comparisons are made cannot be overemphasized.

The cross-correlation method may be most appropriate for evaluating the timing of the peak EMG response rather than the onset of the response as measured in this study. Although the cross-correlation function uses every data point from both signals, the function is most related to identifying peak-to-peak differences between signals. The

peak EMG often occurred when the rate of force was greatest, which follows the initiation of positive rate of force, and results in a smaller activation onset delay than the double-threshold method. Contrasted with timing and muscle "on" measures, the peak EMG response may represent a summation of the neuromuscular response. Because the amplitude of the EMG signal is used as a measure of neural drive to the muscle and is proportional to the number of motor units activated (Kamen & Gabriel 2010), the peak amplitude of the EMG response may be an indicator of the aggregate physiological response to the perturbation of manipulation.

When selecting a method for determining activation onset, there are distinct advantages and disadvantages of the double-threshold and the cross-correlation methods. A key advantage of the double-threshold method is that the muscle activity onset delay in relation to force onset is easily visualized and confirmed during the supervision process. However, the steps require more processing time, and inherently contain a higher potential for human influence than the cross-correlation method. Two advantages of the cross-correlation method are: 1) An absence of a seemingly arbitrary threshold to be defined and 2) Less supervision and therefore less influence to human error. A disadvantage of the cross-correlation method is that it accounts for all data points in the trial, and can be more sensitive to extraneous noise in the signal than the double-threshold method. In addition, a 0 value that results from the cross-correlation method can be difficult to interpret. When a 0 value occurs, the data must be examined to determine if the 0 truly indicates no time shift between the 2 signals (i.e. the peaks of the signals were coincident), or if the data are completely uncorrelated. In this data set, we

obtained 6 zero values out of 34 data points (17 onset delays for the MF, 17 onset delays for the ES) from the cross-correlation function. We visually inspected these signals, and determined that each of these did not correspond with coincident peak contact force and peak muscle activity, and they were excluded. The results that were obtained using both methods highlight the necessity of validating quantitative results, regardless of method chosen, by qualitatively examining the raw data alongside the analysis.

Selecting the time at which the force onset occurs can greatly change the activation onset delays values and underscore the importance of reporting the specific methods used to determine all timing variables. The first increase beyond the preload force (Herzog et al. 1999) and estimates of contact acceleration (Colloca et al. 2003) have been used to define the instant of contact force onset in relation to EMG activity. The duration of the contact phase time (time between the onset of positive contact force and peak force) has been reported as 150 msec for thoracic and lumbar manipulations (Herzog 2010). The duration of this force profile could result in calculated muscle activity onset delays that vary by 150 msec depending on which point during the contact force is selected as the onset of force. We defined force onset as the time at which the rate of force became positive which placed the force onset early in the contact. If instead, the time at which the peak force magnitude occurred was chosen as the onset of force, the delays would shift by an average of 236±77 msec. Because mean onset delay was 149 msec for the MF and 252 msec for the ES this shift could result in negative onset delays (EMG activity *before* force onset), which represents a substantial and clinically meaningful shift. The onset of EMG activity following manipulation in this study most

often occurred after the initiation of the contact and prior to the peak force - at some point during the steepest slope of the force profile.

Peak contact forces measured in this investigation (529.5±152.4 N) are comparable with previous investigations that manipulated the lumbosacral area. Triano and Shultz(Triano & Schultz 1997) recorded mean peak forces of 495.0±142.5 N with experienced clinicians, while Triano et al.(Triano et al. 2004) recorded mean peak forces of 321.0±112.6 N with experienced students. The slightly higher peak forces recorded in this study may have been a result of the experimental set up in which forces from the contact hand were estimated using a combined optimized algorithmic method which allows accurate prediction of contact force (3.6±9.1 N, 95% limits of agreement -21.9 to 14.7 N), while maintaining natural contact between the practitioner and the patient (C. Myers et al. 2012); while previous studies reported forces recorded by the force plate in the treatment table. We expected that the forces applied by the contact hand would be higher than the forces recorded by an embedded force plate after transmission through the patient.

There are 3 novel approaches used in this investigation. First, EMG timing was measured during a side-lying diversified lumbar manipulation as opposed to a prone thoracic maneuver or instrumented manipulation. Second, this is the first investigation that recorded EMG directly from the MF *during* the HVLA manipulation. A recent case study used needle EMG to demonstrate a decrease in amplitude following SM (Tunnell 2009), but the recording occurred following the manipulation and did not address timing.

Because surface EMG recordings are more susceptible to mechanical artifact and confounding crosstalk than indwelling EMG recordings, surface EMG may not represent the activity of the muscle under investigation with complete accuracy (Türker 1993) and it has been recommended that the use of indwelling electrodes is necessary (Stokes et al. 2003) to measure the MF. Last, the contact force of the practitioner was estimated using an optimized estimation technique described by Myers et al (C. Myers et al. 2012). Three-dimensional quantification of side posture contact kinetics is complex, which is why the majority of contact kinetics studies have used a prone thoracic technique (Downie et al. 2010). This technique allows the contact force to be estimated accurately while allowing clinical contact with the practitioner's hand.

Two limitations should be considered when interpreting the results of this study. First, the double-threshold parameter recommendations and comparison of methods and results are generalizable only to muscle activity during spinal manipulation. Second, the L3 manipulations analyzed in this study were part of a larger treatment data set that included an SI manipulation. Although the order of treatments was randomized, there may be an effect of treatment order on muscle activity. Future work using these data will compare painful and non-painful participants, additional deep and superficial lumbar muscles, treatment locations, different manual treatment types, and further establish the neuromuscular relation of muscle activity to contact force during these procedures.

4.5 Conclusion

A comparison of 2 methods for onset detection, double-threshold and cross-correlation, is presented that combines optimized contact force estimation with EMG recordings. We recommend the use of the double-threshold method with an 8 SD amplitude and a 10 msec duration threshold as the method that best represents the EMG timing response to manipulation. The interpretation of onset delays is critically dependent on criteria used to determine the onset of the force application and should be reported in future studies. These methods improve upon previous applications, add to the current catalogue on muscle activation and can provide a basis for standardizing timing calculations across investigations and gain further insight into the neuromuscular effects of the spinal manipulation.

CHAPTER 5. THE BIOMECHANICAL QUANTIFICATION OF SPINAL MANIPULATION

5.1 Spinal Manipulation Quantification

The quantification of SM has a relatively short history compared to the biomechanical study of other medical interventions. A literature synthesis revealed 31 studies that contained quantitative data of the biomechanical properties of manipulation and outlined the state of the literature as it relates to quantitative data on the biomechanical properties of SM (Triano 2001). The review concluded that the biomechanical parameters of SM could be quantified and used to form a system to test hypotheses of treatment effect. This promotion of a systematic approach to the classification of spinal manipulation has important clinical ramifications. A "state of the art" paper on basic science related to SM (Cramer et al. 2006) was written with the goal of determining a categorization system for SM. Topic areas of anatomy, biomechanics, somatic nervous system, animal models, immune system, and human studies related to the autonomic nervous system were included to better define future research directions. Both the literature synthesis (Triano 2001) and the white paper (Cramer et al. 2006) recommended the implementation of a classification system in order to better define the research problems and clinical implications of SM.

Past in-vivo research has primarily focused on mechanical responses of to manipulation such as external force application, vertebral movement, and cavitation. External contact forces, which quantify the forces exerted by the practitioner on the patient, have been quantified using force platforms (Triano & Schultz 1997; Kirstukas & Backman 1999; Tsung et al. 2005), pressure mats(Herzog, Conway, et al. 1993), and a combination of instrumentation (C. Myers et al. 2012). Relative translation of vertebral bodies and zygapophyseal joint movement has been characterized using bone pins in cadavers (Gal et al. 1997), modeled (Keller & Colloca 2002) and imaged using techniques such as MRI (Cramer et al. 2000). Facet joint cavitation caused by manipulation has been recorded and modeled (Herzog, Zhang, et al. 1993; Conway et al. 1993; Evans & Breen 2006). These measurements have been used to generate a detailed structural understanding of SM, and have proven applicable to training chiropractic students and making clinical decisions.

5.2 Practitioner Contact Force

To produce a neuromuscular response from manipulation, a mechanical event must occur. The kinetics of the mechanical HVLA thrust have been measured with the goal of describing the phases of the manipulation impulse including preload, thrust velocity, and peak force (Triano and Schultz 1997; Triano 2001). These characteristics can be measured directly using sensing devices between the practitioner and participant, or indirectly using force-sensing devices located outside the practitioner-participant interaction. Triano et al (1997) performed the seminal work in the field of manipulation

quantification and estimated loads experienced by the spine during manipulation using inverse dynamics from a sensing device embedded in the table. A common problem encountered when measuring the forces of manipulation is the variability of the force applied by the practitioner. This variability can be a result of many factors including contact area, hand position, anthropomorphic differences, and technique (Downie et al. 2010). A novel technique that uses both direct and indirect measures of contact force measurement combined into a single mathematical framework was developed (Myers et al., 2012). Using a weighted least squares approach the clinician's treating contact force can be predicted during manipulation. These methods allow the clinically relevant contact points to be preserved, while including additional contact points such as the patient's shoulder and thigh allowing a complete description of the kinetics. These advances in instrumentation and computational refinement show promise for the improvement and standardization of quantification methods.

The high velocity low amplitude SM, is a specific manipulative technique designed to restore motion to spinal segments. Lumbar HVLA is a commonly used technique that is generally applied to the low back in the side-lying position. The force-time profile for the HVLA thrust can be subdivided into several components: 1) a preload phase in which a quasi-static load is applied to the soft tissues, 2) a "run-up" in which the contact force is lessened just prior to the thrust, 3) the high velocity low amplitude thrust, 4) the peak force exerted into a joint, and 5) the total thrust duration as measured from the bottom of the run-up to the time of peak force (Downie et al. 2010) (fig. 5.1).

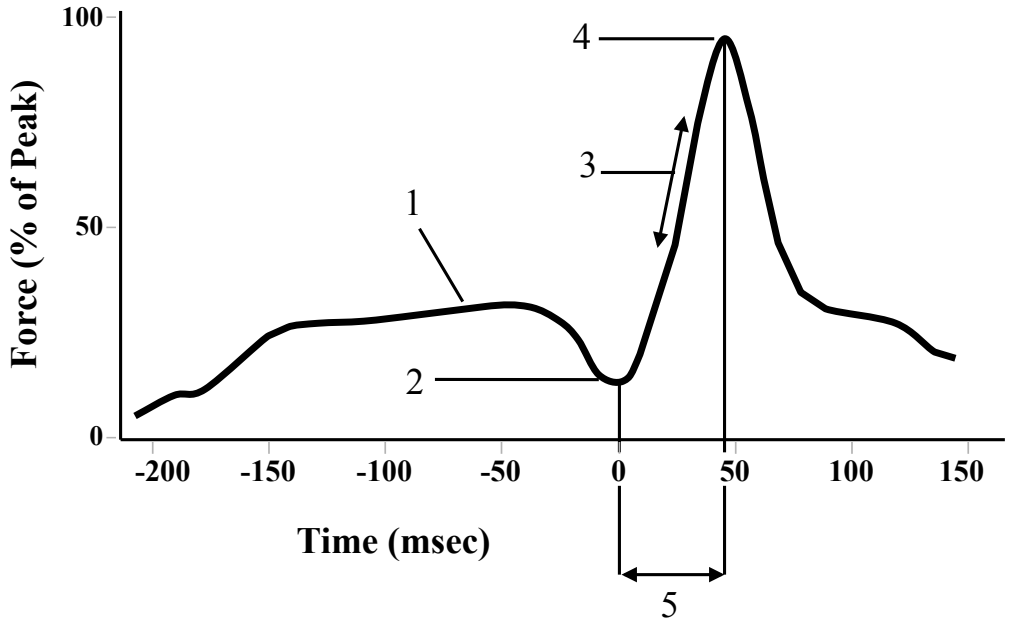

Figure 5.1. Components of the HVLA force: 1) Preload, 2) Run-up, 3) Thrust Speed, 4) Peak Force, and 5) Total Duration. *Source*: Data adapted from Downie 2010, figure 1.

The first attempt to quantify loads during a lumbar SM using inverse dynamics in a clinical setting, positioned subjects on a specially constructed table capable of sensing forces and moments about three axes (Triano and Schultz, 1997). EMG data of the lumbar musculature was recorded using surface recording electrodes, which served as the input to a biomechanical model that estimated the loads passing through the spine. The the loads experienced by the spine during manipulation were comparable with common occupational loads - likely below injury threshold. Limitations included a force platform that may not have fully quantified the forces involved and the inherent limitations of surface EMG. A more recent review described forces exerted by chiropractors during an HLVA and addressed relative movements, reflex responses, safety issues related to forces applied to the soft tissues (including the vertebral artery) and the role of the audible

release (Herzog 2010) and concluded that there is little knowledge of stresses and strains across hard and soft tissues during spinal manipulation. The complexity of measuring forces in three dimensions and the inaccessibility of internal structures such as the spine continue to contribute to this knowledge gap.

5.3 Vertebral Motion

The measurement of vertebral motion in response to manipulation is of primary relevance given the clinical goal of restoration of abnormal joint motion. The vertebral motions and neuromuscular responses to mechanical force have been investigated using patients who underwent lumbar laminarthrectomy (Keller et al. 2003). The goal was to quantify vertebral motions in response to short-lever spinal manipulative thrusts using an instrument. The results showed that although the neurophysiological response was variable from patient to patient, the manipulations resulted in measureable biomechanical and neurophysiologic responses that were temporally related to the applied force during a SM suggesting that the motions play a prominent role in eliciting responses. Limitations of this study include the neurologic deficits in the participants and the small sample size (n=4).

Spinal manipulation and its effect on the motion of facet joints was investigated using displacement controlled motions and recording vertebral strains and motions in cadaveric spine specimens(Ianuzzi & Khalsa 2005). The goal was to determine whether human facet strains during simulated manipulation were different than those that occur during physiological motions. Paraspinal tissues were removed and reactions to SM from

the muscles such as the multifidus could not be considered. Vertebral kinematics and capsule strains were measured resulting in quantification of loads, translations and rotations of the spine and facet joints. This study concluded that during SM facet joint capsule strain magnitudes were at the high end of the range that occurs during physiological motions and thus SM is likely a biomechanically safe procedure.

Cadavers have been used to study SM and the movement of the adjacent vertebral segments with respect to each other (Gál et al. 1997). This line of investigation is important in uncovering whether the underlying clinical assumption of increased joint motion after treatment are valid. The motion between targeted and immediately adjacent vertebrae was measured during manipulative thrusts. In addition to the relative motions measured, it was shown that vertebral pairs remained slightly 'hyper-extended' after the forces had returned to preload levels. This has clinical implications with regard to the lasting effects of the manipulation. Furthering the concept of improved vertebral body measurements, bone pin measurements have been compared to less invasive measures (Gal et al. 1997). No significant differences were found between the posterior-to-anterior translations of vertebrae obtained from the surface markers as compared to the bone pins.

Imaging techniques have been used to quantify the motion of the facet (zygapophyseal) joints of the lumbar spine revealing increased separation (gapping) of the joints during SM (Cramer et al. 2002). Side-posture positioning also produced gapping, but less than that seen with an HVLA lumbar side-posture manipulation. Zygapophyseal joints receiving SM gapped more than those receiving side posture positioning alone; joints of men gapped more than those of women, and cavitation

indicated that a joint had gapped but not how much a joint had gapped (Cramer et al. 2012). These studies confirmed the hypothesis that motion of the facet joints is involved in SM.

5.4 Modeling

The creation of valid and detailed models of the lumbar spine is an important tool in the pursuit of biomechanical quantification of SM. The dynamic response of the lumbar spine using the kinematic response to static and dynamic forces has been investigated using a two-dimensional model analysis (Keller & Colloca 2002). A model was developed to predict the posterior to anterior movement of the lumbar spine during SM. Equations of motion were solved and compared for both mobilization and 2 types of SM. The authors concluded that this simple model, based on an assemblage of homogeneous rigid masses (vertebrae) connected by flexible linkages, could be used to predict the posterior to anterior displacement response of the lumbar spine. Limitations of the model included that only posterior to anterior motions in response to posterior to anterior thrusts could be determined; the model tended to underestimate the motion response in very low-loading or high-loading situations; and that the influence of the thorax and pelvis were not considered. While this model provides important information, its primary limitation is that it models two dimensional forces in the lumbar spine while the typical application of SM to the lumbar spine involves three-dimensional loads and moments.

In addition to the two-dimensional model discussed above, a linear three-dimensional finite element model was developed to predict the vertebral displacements resulting from a manipulative force applied to the lumbar spine (Lee et al. 1995). The complete model included ribcage, the thoraco-lumbar spine and the pelvis with associated soft tissues. This model was found to be useful for the prediction of slowly applied lumbar posterior to anterior forces but was limited in that only posterior to anterior forces were able to be considered and may be limited in the modeling of a high velocity mechanical events such as the HVLA SM.

5.5 Treatment and Response Factors

SM performed at different spinal levels (lumbar, thoracic, cervical) of the spine is mechanically distinct. While manipulation is often performed to the lumbar spine, studies of SM have often involved the thoracic spine for practical reasons. The thoracic spine involves primarily a posterior to anterior thrust, perpendicular to the patient and table or sensing device, while the lumbar spine involves more complicated three-dimensional forces and moments. In a 2010 review of the literature (Downie, 2010) it was noted that out of 27 studies on the forces involved in an HVLA, only three were performed in the lumbar spine.

SM is performed in many different ways, in different locations, with different instruments. There are different clinical evaluation methods used, and little evidence that one evaluation method is advantageous over another (Triano et al. 2013). Treatments are often performed in different positions, over multiple treatment sites, and over variable

amounts of time. The outcome studies performed to date have not routinely measured kinematics or biomechanical outcomes and no standard exists for reporting this information (Downie et al. 2010). Even the need for specificity is questioned as current evidence suggests SM is effective regardless of the technique provided, as long as the appropriate patient is chosen (Cleland et al. 2009). Clarity in these findings is needed to determine whether the specific mechanical variables and location of SM are relevant or whether simply providing a thrust to the proper patient is adequate (Bialosky et al. 2011)

Neuromuscular responses to SM as measured by EMG have been correlated to the side of the force application and found in sites distant from that of the applied force, but these effects were seen in some participants and not others (Herzog, Scheele, and Conway 1999). In addition, treatments on the left side of the subject resulted in a far less number of responses than a treatment on the right side of the body (Herzog, Scheele, and Conway 1999) . These findings remain unexplained. In a clinical setting multiple manipulations are often performed in the same treatment session, however the effect of treatment order is largely unexplored. For example, Herzog (Herzog, Scheele, and Conway 1999) used 11 treatments per subject - administered in a set order - and it was not clear if there was an effect of order on the neuromuscular response. While providing a solid foundation on which to build, studies have lacked broadness to draw associations between the treatment variables of manipulation and the intended responses.

The neuromuscular response to manipulation is produced by clinicians in a variable setting and it is currently unclear how treatment-specific variables influence the neuromuscular response. Variables that have both clinical relevance and a theoretical

foundation for further exploration include: manipulation location, manipulation order, and muscles affected (layer, location, and side). Identifying variables that affect the physiological outcomes of manipulation will assist in the development of a more coherent model for treatment application.

CHAPTER 6: TREATMENT AND RESPONSE FACTORS IN MUSCLE ACTIVATION DURING A SPINAL MANIPULATION

6.1 Introduction

Low back pain is the second most common cause for visits to a primary care physician (Deyo et al. 2006). It is a significant financial burden with medical expenses, missed work and reduced performance accounting for billions of dollars in annual costs (Stewart et al. 2003). Spinal manipulation is a cost-effective treatment when used alone or in combination with other techniques (Michaleff et al. 2012), and is an accepted treatment for low back pain (Bigos & Bowyer 1994). The forces produced during an SM have been shown to induce individual vertebral motion, increase facet joint gapping, changes in intradiscal pressure, changes in pain thresholds, and changes in paraspinal muscle activity (Maigne & Vautravers 2003). Changes in muscle activity, as measured by EMG is a measure of the neuromuscular response to SM which is thought to play a role in its pain reduction mechanism (Pickar 2002). Measures of the neuromuscular response have not produced consistent results across research studies (Lehman 2012) as both reductions in resting EMG activity (DeVocht et al. 2005) and excitatory effects (Dunning & Rushton 2009) have been observed. A better understanding of the varying neuromuscular responses observed during SM leads to improved mechanistic understanding and clinical delivery.

Quantification of SM within basic science research that translates to a clinical setting is challenging, as the study of manipulation lacks a strong history of systematic quantification of the biomechanical factors involved. There are two primary factors that affect research designs when investigating the neuromuscular response to SM: 1) *Treatment Factors* and 2) *Response Factors*. Treatment Factors are variables that are chosen by the practitioner and include the order of the manipulations performed, and the location of the applied treatment. Response Factors are variables in the neuromuscular response and include the muscle layer, the location of the muscle, and the side of the muscular response. The effect of these factors, which are sparsely reported in the manipulation literature, could help explain the variable results observed across studies. A systematic quantification of these factors could not be found.

It is currently unclear how the order of treatments performed to similar areas of the spine affects the neuromuscular response. Equipment set up, data acquisition time, and participant comfort considerations often lead to study designs where multiple manipulations are performed in an effort to maximize valuable time in the laboratory. Multiple manipulations are performed to the same sites, sometimes as many as 16 (Colloca et al. 2003). In other cases, manipulations are repeated until a desirable result is achieved (Herzog et al. 1999). These designs replicate how SM is delivered in a clinical setting, often performed repeatedly and at multiple sites during the same visit.

The location of the manipulation may affect the location of the muscle response (Herzog et al. 1999). Understanding how manipulation location affects the neuromuscular response in healthy people is necessary to establish baseline values for future work in

painful participants. A wide variety of methods are used to determine where to administer the SM (Triano et al. 2013) and a manipulation that is applied to a painful spinal segment results in muscle activity reductions that is not seen in non-painful spinal segments (Lehman & McGill 2001) This finding of different responses at painful sites has led to an emphasis on measuring the response to SM in clinically relevant painful areas (Lehman 2012). This approach has the advantage that the manipulation is applied to a clinically relevant area, but leaves the choice of location to the practitioner, varies from participant to participant within a given study, and presents difficulties in comparing results across participants. Understanding how the location of the applied manipulation force affects the neuromuscular response helps inform both clinical delivery and research design.

Potential Response Factors include the layer, location, and side of the responding muscle. Muscles in different layers perform different functions. The prevailing view of low back muscles is that the superficial erector spinae are broad movers of the trunk while the deep multifidi are important for segmental control (Macintosh & Bogduk 1986). Reductions in multifidus activity has been found in patients with LBP that was not observed in the erector spinae (Danneels et al. 2002). These muscles perform different functions and behave differently in the presence of LBP, underscoring the importance of understanding the effect of SM on these different muscle layers. The rate of the neuromuscular response appears to relate to the muscle's distance from the manipulation location (Herzog 2010). Neuromuscular responses to SM have been found in sites distant from that of the applied force, but these effects were seen in some participants and not others (Herzog, Scheele, and Conway 1999); and the rate of muscle spindle firing is

increased when manipulation forces are directed closer to the recording spinal level in feline specimens (Reed et al. 2015). Spinal manipulation is often applied asymmetrically - especially in the lumbar spine and pelvis - and differences in the response rate on the left and right side of the body have been seen during manipulations directed at the lumbar spine and SI joint. (Herzog et al. 1999). Specifically, treatments on the left side of the subject resulted in a far less number of responses than a treatment on the right side of the body (Herzog, Scheele, and Conway 1999). These findings remain unexplained.

Indwelling EMG is the method of choice for quantifying the activity of the multifidus (Stokes et al. 2003); however, investigations of the activity of the multifidus *during* a spinal manipulation have not been carried out. Spinal manipulation is thought to alter neuromuscular activity in the paraspinal muscles (Pickar 2002), with the pioneering work being performed in the erector spinae (Herzog, P. Conway, et al. 1995; Herzog et al. 1999). Increased erector spinae activity during a maximal voluntary contraction following SM compared to pre-SM activity was demonstrated in a clinical trial (Keller & Colloca 2000); however, the effect of SM on the activity of the multifidus has been limited to case reports. Increases in multifidus activity (Tunnell 2009) and thickness (Brenner 2007; Koppenhaver et al. 2012) were demonstrated following SM, implying a link to multifidus function.

The goal of this study was to quantify the effect of treatment factors (manipulation order and location) and response factors (muscle layer, location and side) on two dependent variables of interest: 1) the muscle response, which is the percentage of muscles that respond to SM, and 2) the muscle activity onset delay, which is a timing

variable. Eight different muscles in two different layers of the low back were recorded during a spinal manipulation. Quantifying the differences in these responses will lead to improved study design, better clinical delivery, and contribute to a better understanding of the mechanisms of this treatment.

6.2 Methods

6.2.1 Participant information

Twenty participants (table 6.1), each with no history of low back pain during the previous four years visited the laboratory for a single test session that lasted three to four hours during which muscle activity was collected from the low back during SM. An orthopedic and neurologic examination was performed to screen participants for contraindications to SM including radicular pain below the knee, sensation, or weakness in the lower extremity, or a pain level that exceeded a seven out of ten on a verbal pain scale. Written, informed consent in accordance with the institutional review board was obtained prior to the start of the testing session (see Appendix C for more participant information).

Table 6.1. Mean ± SD participant anthropometric information.

	Male (n=10)	**Female (n=10)**
Age (years)	33.4 ± 13.9	31.8 ± 7.9
Height (cm)	179.3 ± 7.3	165.0 ± 2.9
Weight (kg)	79.3 ± 9.0	60.2 ± 5.0
Dominant Hand (right/left)	(9/1)	(8/2)

6.2.2 Application of spinal manipulation

Two lumbar diversified side-lying HVLA manipulations and two grade IV mobilizations were performed on each participant by one of two chiropractors, each with over 10 years of experience. One manipulation and one mobilization was performed at the L3 spinal level and one at the SI level, using a hypothenar hand contact. HVLA manipulations consisted of a single quick force, while the mobilizations consisted of 5 slower, less forceful rocking motions delivered at a frequency of 1Hz. The order of treatments was randomized, the time between the treatments was between 1 and 3 minutes and only the data from the HVLA manipulations was used in this analysis.

6.2.3 EMG and force instrumentation during manipulation

Eight EMG electrode pairs were used to record signals from the low back. Four surface electrodes were used, recording muscle activity from the erector spinae (bilaterally at the L2 spinal level), the lower trapezius (left), and the quadratus lumborum (left). Four indwelling electrodes (50mm, 25ga needle for insertion, with a pair of 0.051mm, insulated, hooked wires and 200mm tail with 5mm bare-wire terminations) recorded muscle activity from the multifidi (L2 and L5 bilaterally) and were inserted 2.5 cm lateral and 1 cm superior to the tip of the spinous process at a 45 degree angle towards the spine (Haig et al. 1991). A Noraxon TeleMyo DTS (Noraxon USA, Scottsdale AZ) system was used to record both surface and indwelling EMG signals. The force from the practitioner's contact hand was estimated using an optimized algorithm that combines measurements from force transducers attached to the practitioner with measurements

from a force plate (Bertec Corporation, Columbus, OH) embedded in the treatment table and allows the maintenance of natural contact between the practitioner and the participant(C. Myers et al. 2012) (fig. 6.1).

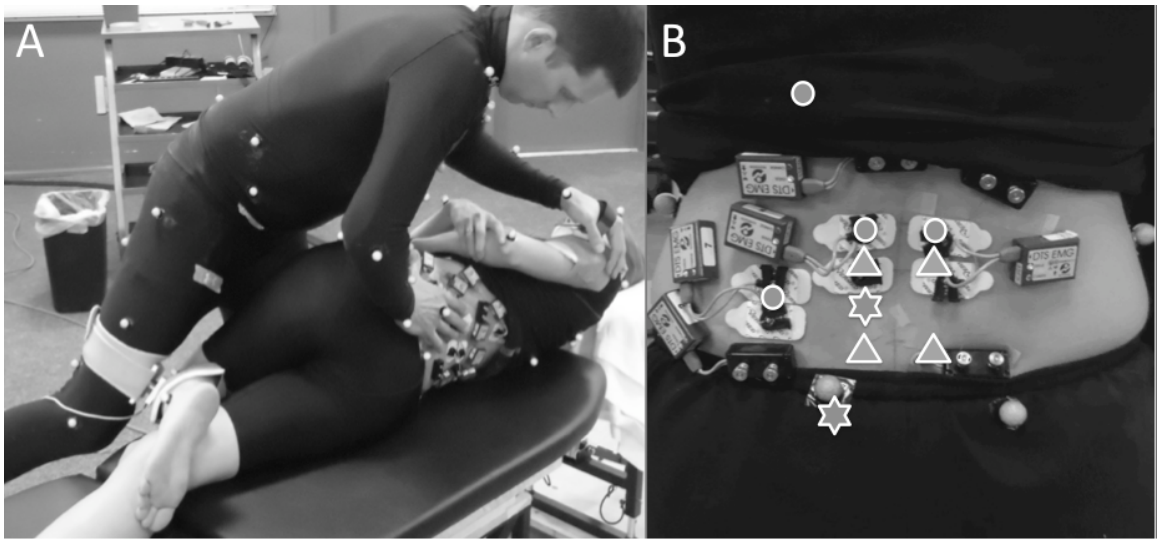

Figure 6.1. A) Side posture set-up B) Instrumentation included indwelling (triangles) and surface (circles) EMG. Stars indicate manipulation sites at the L3 and SI spinal level on the left.

6.2.4 EMG signal processing

Movement artifact and high frequency noise were removed from the raw EMG signals with a bandpass filter (4th order Butterworth, 15-350Hz). Signals were transformed using the TKEO which improves muscle activity onset detection (Li et al. 2007; Solnik et al. 2008) (equation 3.1).

6.2.5 Muscle response and muscle activity onset delay

Presence of a muscle response was determined with a double-threshold method that contained amplitude and duration components optimized specifically for HVLA

manipulations (see Chapter 4 and Appendix A.4). Muscle response was calculated by recording the number of locations with a response and dividing by the total number of muscle locations evaluated, expressed as a percentage.

$$Muscle\ Response = \frac{\#\ of\ Positive\ Responses}{\#\ of\ Muscle\ Locations}\ X\ 100 \qquad 6.1$$

Muscle activity onset delay, which is a timing variable was calculated as the time delay between the first positive slope of the manipulation force and the first energy transformed EMG activity that resulted in a muscle response.

6.2.6 Analysis of Treatment Factors and Response Factors

Analysis of dependent variables was separated into two categories: 1) Treatment Factors, which focus on how the SM was applied; and 2) Response Factors, which focus on the type and location of the muscles that respond to the SM.

The effect of the Treatment Factors including order (first or second) and manipulation location (L3 or SI) on the number of muscle responses and the muscle activity onset delays were compared using mixed-model linear regressions with a random effect for subject. Equivalence between the first and second manipulation was determined for both muscle response and muscle activity onset delay by using a varying practical difference threshold until equivalence was achieved.

The effect of the Response Factors including muscle location (indwelling L2, L5, surface L2, QL and Trap), muscle layer (multifidus or superficial), and muscle side (left

or right) on the number of muscle responses and the muscle activity onset delays were compared using mixed model linear regression with a random effect for subject. Only muscles with a contralateral analog were used for right and left comparisons (L2 multifidus, L5 multifidus, and L2 erector spinae). Effect sizes for all comparisons were calculated using Cohen's *d*. A small effect was defined as $0.2<d\leq0.5$, a moderate effect as $0.51\leq d\leq0.79$, and a large effect as $d\geq0.8$ (see appendix A.5 for statistic methods background).

6.3 Results

6.3.1 Treatment Factors

6.3.1.1 Manipulation Order

A response occurred in 67.5±26.7% of the first manipulations, and 55.6±29.9% of the second manipulations. The effect size of manipulation order was small (d=0.42), and the difference was not statistically significant (β=-11.8%, SE=7.1%, p=0.11). Where β is the model-predicted regression offset of the second manipulation, a negative β value indicates a lower value for the second manipulation. There was no effect size and no statistically significant difference in the muscle activity onset delays between the first and second manipulation (β=-10.1msec, SE=11.7msec, p=0.35). Equivalence testing revealed the first and second manipulations were equivalent at the 28% practical difference threshold for the muscle response, and equivalent at the 30 msec practical difference threshold for the muscle activity onset delays.

6.3.1.2 Manipulation Location

For all muscle sites, a response occurred in 65.6±24.3% of the L3 manipulations, and 57.5±32.5% of the second manipulations. The effect size of manipulation location was small (d=0.29), and the difference was not statistically significant (β=-4.1%, SE=3.7%, p=0.28) where β is the model-predicted regression offset of the SI manipulation. There was no effect size and no statistically significant difference in the muscle activity onset delays in all muscles between the L3 and SI Manipulation (β=-5.5msec, SE=5.8msec, p=0.35).

6.3.2 Response Factors

6.3.2.1 Muscle Layer

There was a small effect size (d=0.20) and no statistical difference between the multifidus and superficial muscles in the number of muscle responses (β=3.4%, SE=2.83%, p=0.23). There was a small effect size (d=0.25) and significantly shorter muscle activity onset delays in the multifidi than in the superficial muscles (β=-13.0msec, SE=5.6msec, p=0.02). (fig. 6.2)

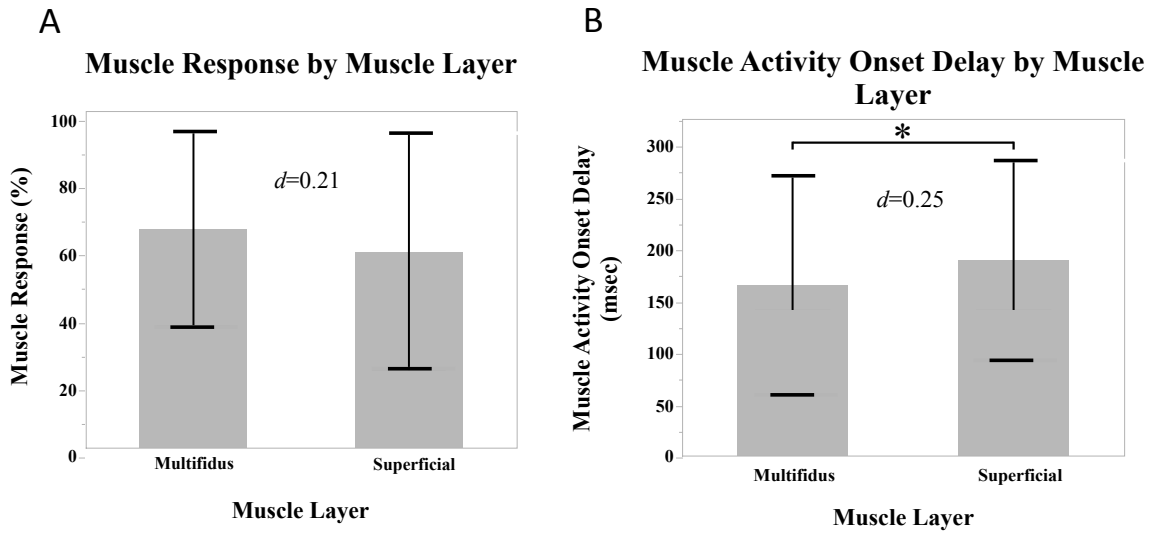

Figure 6.2. Mean muscle responses (A) and mean muscle activity onset delay (B) for the multifidus and superficial muscles. Stars indicate a statistically significant difference.

6.3.2.2 Muscle Location

A greater number of responses occurred in the L5 indwelling location on the left compared to the other muscle locations (β=18.4%, SE=6.5%, p=0.047). Shorter muscle activity onset delays occurred in the L2 (β=-27.7msec, SE=13.9msec, p=0.047) and L5 (β=55.9msec, SE=12.8msec, p=0.001) indwelling electrodes on the left, and longer delays occurred in the L5 indwelling electrode on the right (β=38.8msec, SE=14.4msec, p=0.01) (fig. 6.3). The muscle response and the muscle activity onset delays revealed patterns relating to their anatomical location and the treatment location (fig. 6.4).

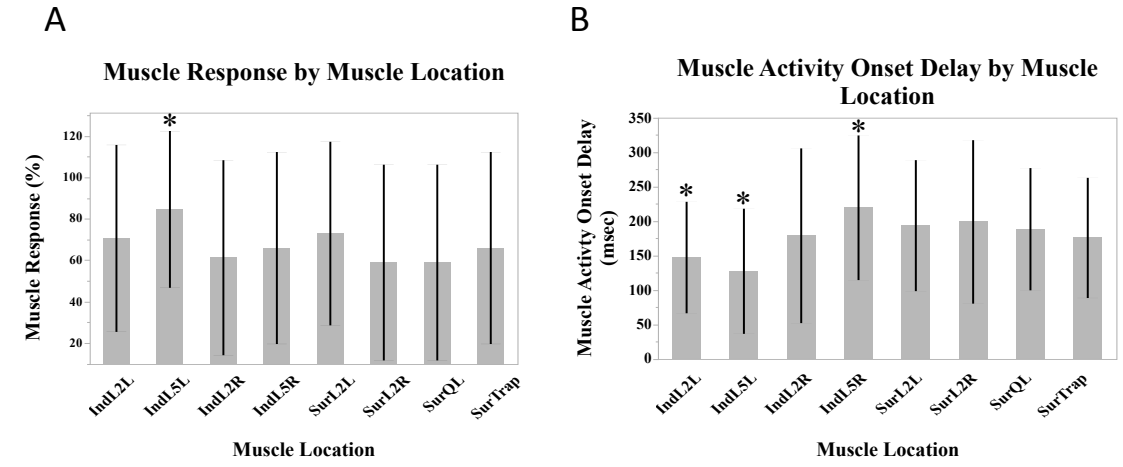

Figure 6.3. Mean muscle responses (A) and mean muscle activity onset delays (B) across all muscle locations. Stars indicate statistically significant differences from the mean.

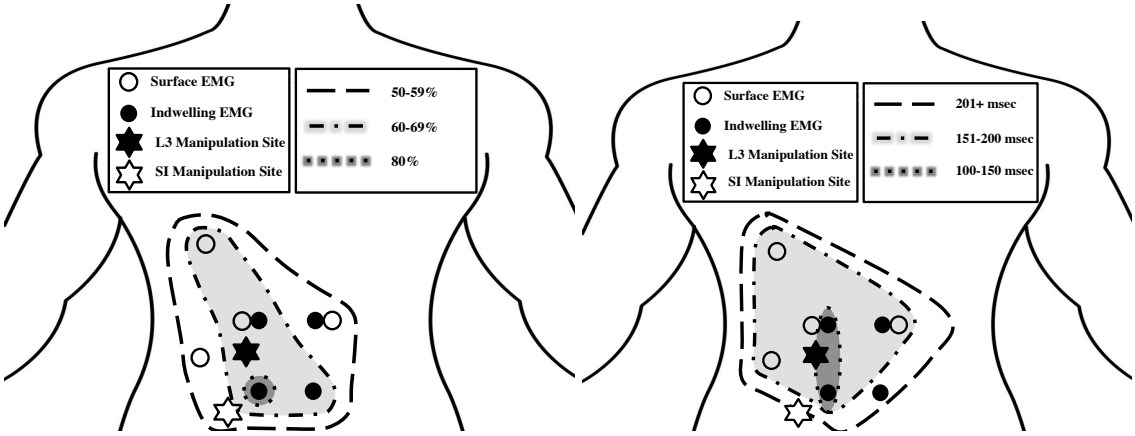

Figure 6.4. Anatomical distribution of muscle responses (A) and muscle activity onset delays (B) for all 8 muscle locations in relation to the manipulation locations (indicated by stars).

6.3.2.3 Muscle Side

There was a small effect size of side on muscle response (d=0.44) and a greater number of responses in the muscles on the left side than the right side (β=7.5%, SE=3.0%, p=0.02). There was a small effect size (d=0.44) and significantly shorter

muscle activity onset delays in the muscles on the left side compared with the right (β=-23.0msec, SE=6.7msec, p<0.001) (fig. 6.5).

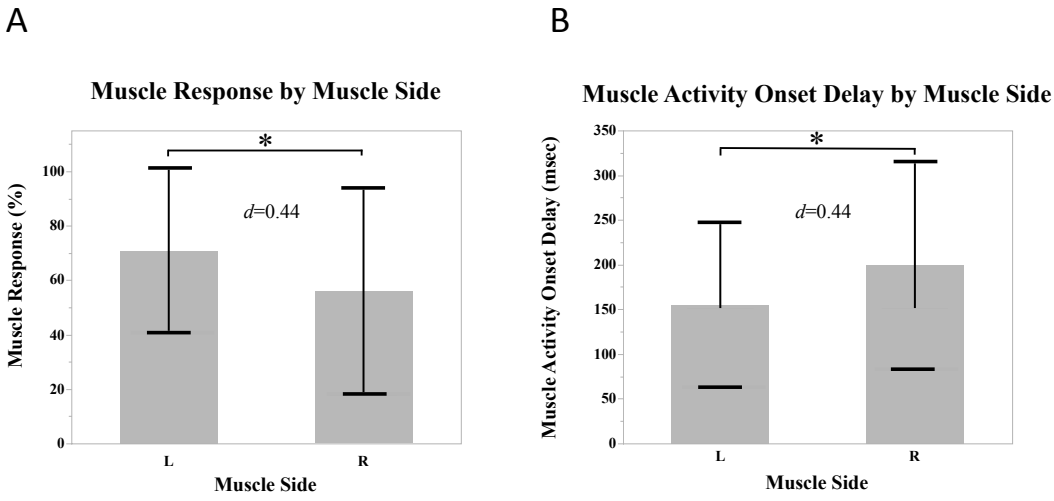

Figure 6.5. Mean muscle responses (A) and mean muscle activity onset delay (B) for the on the left and right side. Stars indicate a statistically significant difference.

6.4 Discussion

This study quantified the effects of treatment factors and response factors on the neuromuscular response to SM as measured by the rate of muscle response and the muscle activity onset delay. The goal was to establish factors that may have an effect on the response using a standardized method (see chapter 4) and to quantify responses in a healthy population *during* a spinal manipulation. These results suggest future studies and clinical treatment focused on timing outcomes can be designed without regard for manipulation order (separated by at least 3 minutes) and location (within in the lumbar region), whereas studies focused on the number of muscle responses may want to consider these variables due to the small effects noted.

The lack of statistically significant difference between the first and second manipulations could be viewed as an indicator of confidence in the repeatability of the measures; noteworthy however the muscle response was equivalent at a 28% difference threshold which is large enough to be impractical for considering these responses equivalent, and the muscle activity onset delays could be considered equivalent at the practical level of 30 msec. This is consistent with the finding of a small effect of order for the muscle responses and no effect on the muscle activity onset delays. In this study, the first and second manipulations were separated by 1-3 minutes and were in close anatomic proximity (L3 and SI). Although we were unable to locate investigations on reliability for EMG measures in the spinal manipulation literature, within-session reliability for EMG measures in the low back during active tasks has shown to be moderate to high using alpha coefficients (Watson et al. 1997). The activation of a motor unit depends on variable factors including the type of muscle, training level of the participant, and fatigue state of the muscle (G. L. Soderberg & Knutson 2000), making comparison across days and muscle groups difficult (Lehman & Mcgill 1999). This study was not statistically powered to see statistical differences between first and second manipulations, but consideration for an effect order in future studies should be considered, especially those concerned with the number of muscle responses.

The lack of statistical difference in the neuromuscular responses during SM performed at different locations demonstrate that specificity of the contact site may not play a major role in biomechanical outcomes. The close proximity of the two manipulation locations may explain the lack of differences seen in this study and is

consistent with other location variables analyzed during SM. Previous work has found no difference in responses such as joint cavitation regardless of whether the manipulation was directed at the L5 or SI joint (Beffa & Mathews 2004); that responses can occur above and below the targeted joint (Ross et al. 2004); and that hand configuration can lead to forces being applied to levels other than the targeted vertebrae (Perle & Kawchuk 2005). Given the broad spinal, pelvic, and thigh motions produced during a side-lying manipulation and the size of the hand contact relative to the anatomical structures being manipulated, it is not surprising that the neuromuscular responses are not affected by a small difference in a single contact point.

This study confirms a previously undocumented response in the multifidus *during* a side-lying SM. The shorter onset delays in the multifidus indicates a faster response than the erector spinae and that this muscle cannot be considered similar to others for comparisons across research studies. Previous work has focused on the muscle response of the erector spinae as it is relatively easy to measure, leaving gaps in knowledge regarding deeper muscles such as the multifidus which are important for spinal stability. Because of its deep location and proximity to the vertebral bodies that are a target of spinal manipulation, the multifidus may be the first muscle to respond to SM. The increased responses and shorter onset delays seen in the multifidus may be a characteristic of this healthy population, and future comparisons to participants in pain are warranted to determine if SM could play a role in multifidus activation.

The trend of a greater a muscle response and longer muscle activity onset delays as measurements moved farther away from the site of manipulation (fig. 6.4) indicates a

special relationship of muscle response to manipulation. Muscle responses at distant locations were present which is consistent with previous findings in lumbar and SI manipulations using surface EMG (Herzog et al. 1999); however this work adds the relation of muscle response and muscle activity onset delays to manipulation location which was not seen in previous work. This spatial pattern of the left-sided multifidus having the greatest muscle response and the shortest onset delays in the presence of a left-sided manipulation maybe be a result of the addition of the multifidus recordings in this study. The understanding of the neuromuscular response to SM is improved by the identification of a characteristic timing pattern in response to SM allowing future comparisons to participants in pain.

The greater muscle response and shorter delays on the left side compared to the right are consistent with the stretch of the tissues on the upper side during a side-lying manipulation. The left-sided (upside) muscles responded with a greater rate and a faster response, which was consistent with the trend of a greater effect size of SM closer to the treatment site, Interestingly, the multifidi as a whole group did not always have the greater number of responses or the shortest onset delays, but the left sided multifidi did, indicating that the side of the response may have more influence than the layer of the muscle responding (Figure 4). Because of the rotational nature of the side-lying manipulation the upside musculature is likely stretched more than the down side. The upside is also thought to receive the most force and has been shown to produce the most gapping of the facet joints (Cramer et al. 2012). As tissues such as the erector spinae, the multifidus and the facet joint capsules are stretched during a spinal manipulation(Ianuzzi

& Khalsa 2005), the muscle spindles and golgi tendon organs are stimulated (Pickar & Wheeler 2001) causing changes in the neuromuscular response.

In the only previous work using a lumbar side-lying manipulation (Herzog et al. 1999), the down-side muscles were not recorded but a greater number of responses was observed in the right-sided muscles when a treatment was applied to the right side than in the left-sided muscles when a treatment was applied to the left side. During a prone manipulation of an exposed vertebrae with a mechanical instrument the right sided nerve roots produced a greater number of responses (Colloca et al. 2003). Because of the experimental set up used in this study the responses from both sides were able to be measured for direct comparison. A treatment was not applied to the right side, perhaps explaining why we did not have a 100% response rate for any measurement where the previous work did (i.e. we measured the least responsive side). It is unclear if the greater responses on the right side in the previous literature were due to a side dominance of the participant, or a side dominance in the delivery of the manipulation.

A limitation of this study is that the manipulation was not directed at a specific clinical lesion or hypertonic muscle, but rather predetermined by the study design – assigned randomly to the L3 spinal level or the SI. This assignment allowed an unbiased comparison of the muscle responses and timing between standardized treatment sites. Some evidence exists that directing treatment toward a clinical lesion produces less variable EMG amplitude changes (DeVocht et al. 2005) than when one where the treatment was directed directed toward a specific vertebral level (Lehman & McGill 2001).

6.5 Conclusion

Treatment variables (manipulation location and order) had little effect on the neuromuscular response to manipulation. Response variables including the location, layer and side of the neuromuscular response revealed trends of decreasing muscle response rates, and increasing muscle activity onset delays as the distance from the manipulation location increased. Future studies may be designed with this in mind. We anticipate future work to compare subjects in pain, with correlations to clinical outcome measures to aide in the mechanistic understanding of the neuromuscular response to SM.

CHAPTER 7: LOW BACK PAIN AND SPINAL MANIPULATION

7.1 Pain Models in Musculoskeletal Pain

Two primary models have been proposed to explain the muscle activity during musculoskeletal pain syndromes: the pain-spasm-pain model and the pain-adaptation model. The pain-spasm-pain model suggests that the presence of pain leads to a protective muscle spasm, which in turn results in more pain (Travell et al. 1942). There are two neural pathways that contribute to this type of pain cycle. The first is the projections of nociceptive afferents onto excitatory interneurons in the spinal cord, the stimulation of which would cause alpha motor neuron activity and muscle spasm (van Dieën et al. 2003), and the second is nociceptive afferent stimulation of gamma motorneurons which increase muscle spindle output causing increased alpha motor neuron activity and muscle spasm (Johansson & Sojka 1991). Muscles that are activated and remain active, accumulate pain inducing lactate and arachadonic acid thereby closing the pain-spasm-pain loop.

The pain-adaptation model proposes that pain decreases agonist muscle activation and increases antagonist muscle activation (Lund et al. 1991). This strategy is thought to reduce the range and speed of movements thereby acting as a protective mechanism.

The neural pathway suggested as the basis for the pain-adaptation model involves feedback from pain generating nociceptive afferent pathways. Through interneurons in

the spinal cord, these nociceptive afferents can excite or inhibit the alpha motor neurons responsible for muscle activation. This model suggests that this nociceptive feedback inhibits the excitatory signal traveling to the agonist, while simultaneously exciting the inhibitory signal traveling to the antagonist (van Dieën et al. 2003). Evidence for this model has been found in pain induction studies, where muscles are studied after the artificial induction of pain. One such study found increased activity in the gastrocnemius muscle during gait after the induction of pain, and decreased activity of the antagonist tibialis anterior (Graven-Nielsen et al. 1997).

Using these two models to interpret increases or decreases in muscle activity in patients with LBP results in different conclusions. The pain-spasm-pain model predicts an increase in muscle activity as a result of pain to support and protect the injured tissue, and the pain-adaptation model predicts a decrease in activity through a protective mechanism designed to slow movement. Reviews of the literature have found support for both of these models in LBP patients (van Dieën et al. 2003).

7.2 Muscle Activity and Low Back Pain

While the causes of LBP are multifactorial, the muscles of the lumbar spine are thought to play an important role (Ahern et al. 1988). The presence of LBP has been associated with elevated levels of paraspinal muscle tension (Nouwen & Bush 1984), changes in motor performance of lumbar musculature during gait (Arendt-Nielsen et al. 1996), and altered function of trunk muscles during activities (Panjabi 2006).

Historically, there is conflicting evidence regarding the clinical presence of muscle spasm in LBP patients. Paraspinal hypertonicity was observed in 72% of low back pain patients upon their first hospitalization (Nashold & Hrubec 1979); however, muscle spasm was not a consistent finding in a study of 25 LBP patients (Paulett 1944). Predictions from the two pain theories suggest that the paraspinal EMG levels of low back pain patients during higher pain states will be elevated (Arena et al. 1991); however, there is conflicting evidence with regards to the absolute activity of the lumbar musculature with both increases and decreases in EMG amplitude observed in participants with LBP compared to controls (van Dieën et al. 2003). Clinically, the assumption of paraspinal hypertonicity associated with pain pervades, however evidence exists that low back pain patients do not have elevated paraspinal EMG (Nouwen & Bush 1984). In light of these discrepancies in experimental EMG amplitudes, the timing of muscle activity has been investigated. It has been shown that chronic low back pain patients have delayed response of trunk muscles during activities such as task performance (Mok et al. 2011), spinal loading, and anticipation of limb movement (Panjabi 2006)

The multifidus and erector spinae muscles of the lumbar spine are thought to contribute to lumbar spine stability. While both muscles are involved in extension of the spine, the principle action of the multifidus is posterior sagittal rotation on a segmental level (Macintosh & Bogduk 1986). In LBP that results from clinical instability, the multifidus is a focus of treatment. In the absence of a surgically operable lesion, conservative therapy is often recommended as the first choice of treatment, and rehabilitative exercises aimed at the multifidus are commonly prescribed (Maher 2004).

Exercise therapy for the multifidus is based on the premise that segmental control, like that provided by the multifidus (Macintosh & Bogduk 1986) is necessary for spinal stability (Panjabi et al. 1989). The multifidus has a localized reduction in cross sectional area (Hides et al. 2008), atrophy on the side of pain (Hides et al. 1994) and lower activity during postural exercises in patients with LBP (Danneels et al. 2002), supporting the hypothesis that strengthening this muscle may have an effect on LBP. This evidence forms the foundation upon which to explore the relation of the multifidus and pain, with growing evidence of the association between deficits in the lumbar multifidus and low back pain (Dickx et al. 2010).

7.3 Spinal Manipulation, Pain, and Muscle Function

A systematic review on the effect of SM on pain perception using chemical, electrical, mechanical and thermal stimuli concluded that SM demonstrates a favorable effect on pain thresholds (Coronado et al. 2012) supporting the observation that pain processing is influenced by spinal manipulation [Cramer et al., 2006]. Studies have found a decreased sensitivity to thermal pain following spinal manipulation (George et al. 2006) and increases in local skin pain thresholds SM but not a placebo (Terrett & Vernon 1984). Theories to explain the pain-inhibiting effects of SM hypothesize that SM stimulates mechanoreceptors, subsequently activating afferent input that inhibits the transmission of nociceptive input (Boal & Gillette 2004). Inhibition of temporal summation (a measure of increasing pain with a constant stimulus over time) in patients with LBP following SM suggests the mediation of pain through spinal cord dorsal horn

inhibition (J Bialosky et al. 2009). In this way SM acts as a "counter irritant" to pain conduction (George et al. 2006).

It has been shown that mechanical forces can alter the activity of the muscles of the spine (Holm et al. 2002). SM with a mechanical instrument has resulted in a significant increase is maximum voluntary contraction muscle output of the erector spinae as measured by EMG (Keller & Colloca 2000). There is evidence of the effects of SM on the MF, with an improved ability to activate the multifidus following SM (Brenner 2007), and increased multifidus thickness with concurrent improvements in low back related disability scores one week after SM (Koppenhaver et al. 2012). These results are opposed by a case study that found improvements in trunk rotational force but decreases in multifidus activity following SM (Tunnell 2009). In addition to local muscle changes in the spine, distant muscle function changes have been observed including muscle inhibition in knee extensor muscles thought to be involved in anterior knee pain after SI joint SM (Suter et al. 2000). Studies of the influence of SM on the transverse abdominus muscle are conflicting with observations of both improvements in the ability to contract the transverse abdominis following SM (Gill et al. 2007) and no effect of SM on transverse abdominis thickness at rest or during a contraction (Puentedura et al. 2011).

7.4 Classification of Low Back Pain

A lack of consensus on the definition of chronic low back pain (Andersson 1999) has resulted in a wide range of prevalence estimates in the literature. Low back pain that lasts for less than 3 months is considered acute (Parthan et al. 2006) and the International

Association for the Study of Pain defines chronic pain as any pain that lasts longer than three months (Bogduk 1994; Bogduk 1999) Approximately 5-10% of low back pain sufferers go on to develop pain that lasts longer than 3 months. (Parthan et al. 2006). Study designs that attempt to relate benefits of a specific treatment to subclasses of LBP patients are hindered by the inability to adequately identify subclasses of patients.

Conflicting evidence exists with regards to the effectiveness of SM in different patient populations: benefits have been shown in acute pain populations with insufficient data to recommend it as a treatment for chronic pain (Shekelle et al. 1992). SM has been found moderately effective for chronic or subacute pain with benefits over sham or placebo but only fair evidence for small to moderate benefits in acute patients (Chou et al. 2014). Strong evidence has been found for the short-term effectiveness of SM in chronic pain patients (van Tulder et al. 1997). To date, quantitative studies on the effect of manipulation on different patient populations have not been performed (Koppenhaver et al. 2012). Human studies on SM have been performed on either symptomatic or asymptomatic individuals, but not both and it has been proposed that paradoxical findings could be resolved if comparisons are made between these groups (Pickar 2002). In addition to comparisons between patients with LBP and healthy individuals, quantifying the response of the low back musculature to SM in different patient populations would assist in the selection of candidates for manipulative therapy and approximate expectations for improvement.

CHAPTER 8: THE NEUROMUSCULAR RESPONSE TO SPINAL MANIPULATION IN THE PRESENCE OF PAIN

8.1 Introduction

Spinal manipulation is a mechanical treatment that is associated with neurophysiological changes, and increasing our understanding of these mechanisms may help improve clinical delivery and patient outcomes. Clinical evidence supports the use of SM for acute low back pain;(Bigos & Bowyer 1994; Lawrence et al. 2006) however, the etiology of clinical improvement as it relates to the neurophysiological response remains unknown. Several neural effects of manipulation have been observed that include changes in muscle activity, central motor excitability, H-reflexes, and pain processing (Cramer et al. 2006; Pickar 2002). Improving our understanding of how these effects are related to clinical conditions may lead us toward additional insight into the mechanism of SM as a treatment.

Muscle activation is the primary means to assess the neuromuscular response to SM, and gain insight into the neuromuscular pathways. Two aspects of muscle activity are commonly quantified using EMG: 1) amplitude of the signal and 2) timing of the signal. Evidence of EMG amplitude changes in response to manipulation is conflicting, and includes both increases and decreases following SM (Lehman 2012; Lehman & McGill 2001). In addition, amplitude measures are subject to interpretive difficulties

across participants and investigations because they are confounded by the normalization process, which is influenced by the type of muscle studied, training level, and participant motivation (G. Soderberg & Knutson 2000).

The second measure of the neuromuscular response is timing, which quantifies the reflex response of the underlying muscles in the treatment area (Herzog 2010). Onset delay of a muscle in response to SM is too short to be a voluntary activation (Herzog et al. 1999), and may indicate the presence of a spinal reflex. Timing of this reflex in response to manipulation has been documented in wide ranges between two msec and 200 msec after force onset, and is associated with the location and type of manipulation administered (Herzog, P. J. Conway, et al. 1995; Colloca et al. 2003)

If a spinal reflex is present in response to manipulation, quantifying the differences in timing between participants with low back pain (symptomatic) and those without (asymptomatic) will lead to a better understanding of the benefits of spinal manipulation. The presence of low back pain (LBP) alters the activity of trunk muscles during functional activities (Panjabi 2006) and both increases and decreases in EMG amplitude have been noted in participants with LBP compared to controls (van Dieën et al. 2003). In participants with frequent or constant LBP, a greater occurrence of reflex responses to manipulation has been reported in the paraspinal musculature when compared to healthy controls (Colloca & Keller 2001); however, these effects have not been investigated in non-instrumented diversified side-lying style of SM commonly performed in the clinic.

The purpose of this study was to evaluate differences in muscle activity in participants with and without LBP during a side-lying lumbar diversified SM. We hypothesized differences between groups in both the number of muscle responses and muscle activity onset delay. We anticipate these results will encourage more investigations into quantifying the neuromuscular response during SM and foster a better mechanistic understanding of the effects of SM on pain.

8.2 Methods

8.2.1 Participant information

Forty participants were recruited and used to compare the number of muscle responses and muscle activity onset delay during SM. Twenty participants (age: 32.6±11.0 years, mass: 70.5±12.1 kg, height: 172.2±9.1 cm) had no history of low back pain (asymptomatic group), and twenty participants (age: 33.4±9.9 years, mass: 71.3±11.5 kg, height: 167.9±10.2 cm) had a history of low back pain located between the lowest rib and the pelvis (symptomatic group). The symptomatic participants were experiencing pain at the time of testing with an average verbal pain scale 3.3 out of 10; and an average Oswestry disability rating of 23.4% indicating a moderate disability (see Appendix C for additional participant data and Appendix A.6 for a description of clinical outcome measures).

Each participant was screened for contraindications to SM by performing an orthopedic and neurologic examination. Exclusion from the investigation occurred if: 1)

current level of pain exceeded a seven out of ten on a verbal pain scale; 2) radicular pain below the knee during orthopedic testing was present; or 3) a neurologic exam revealed absent reflexes, decreased sensation, or weakness. Each participant provided written, informed consent in accordance with Colorado Multiple Institutional Review Board review board prior to the start of the experimental session.

8.2.2 Application of spinal manipulation

High-velocity, low-amplitude SMs at the L3 and Sacroiliac (SI) spinal level with a hypothenar contact in the side-lying position were applied to each participant (fig 6.1). In addition, two grade IV mobilizations were applied but were not analyzed in this investigation. The order of treatments was randomized, and the time between manipulations was between one and three minutes. Manipulations were performed by two chiropractors, each with over 10 years of clinical experience.

8.2.3 EMG and contact force instrumentation

Bilateral surface EMG was recorded from the erector spinae (ES) at the L2 level. Bilateral indwelling EMG was recorded from the multifidus at the L2 and L5 levels (Haig et al. 1991) and unilateral surface EMG was recorded from the left quadratus lumborum (QL) and the left lower trapezius (LT) for a total of eight EMG recording locations (fig. 6B). The contact force between the chiropractor and the patient at the site of treatment was estimated using an optimized weighted least squares model that combines direct and

indirect measurements of force with an accuracy of 3.6N, and allows natural contact between the practitioner and the patient (C. A. Myers et al. 2012).

8.2.4 EMG signal processing

The raw EMG signals were sampled at 2000 Hz, bandpass filtered to remove movement artifact and high frequency noise (4th order Butterworth, 15-350Hz), and transformed using the TKEO (Li et al. 2007; Solnik et al. 2008). Linear envelopes of the EMG signals were created by applying full-wave rectification and a low-pass filter (4^{th}-order Butterworth, 50Hz cutoff).

8.2.5 Muscle responses and muscle activity onset delay calculations

Whether or not a muscle responded and was considered "on" (positive muscle response) was determined using the double-threshold method with an amplitude threshold of 8 standard deviations (SD) calculated from one second of baseline data, and a duration threshold of 10msec (see Chapter 4). The muscle response variable was calculated by recording the number of positive responses across eight EMG channels and dividing by the total number of channels, expressed as a percentage.

$$Muscle\ Response = \frac{\#\ of\ Positive\ Responses}{\#\ of\ \ EMG\ Channels} X\ 100 \qquad (8.1)$$

Muscle activity onset delay was quantified as the time delay between the positive slope of the manipulation contact force and the first EMG activity that met the previously reported double threshold criterion.

8.2.6 Comparison of asymptomatic and symptomatic participants

Differences in the muscle response and the muscle activity onset delay between the two pain groups (symptomatic and asymptomatic), two electrode types (multifidus and superficial), two manipulation locations (L3 and SI), and manipulation order (first or second manipulation) were compared using mixed linear regressions with a random effect for subject. Effect sizes for all comparisons were calculated using Cohen's *d*. A small effect was defined as $0.2<d<0.5$, a moderate effect as $0.5 \leq d<0.79$, and a large effect as $d \geq 0.8$. Level of significance for all statistical tests was set at $\alpha=0.05$.

8.3 Results

8.3.1 Muscle responses

Muscle responses occurred in 57.2% of all EMG recording sites during spinal manipulation. Across participants, muscle response occurred in 61.6±23.6% of the EMG locations in the asymptomatic group and 52.8±26.3% of the symptomatic group (Figure 2). The effect size was small ($d=0.35$), and the difference was not statistically significant ($\beta=-4.3\%$, SE=3.9%, $p=0.27$) where β is the model-predicted regression offset of the symptomatic group (fig. 8.1).

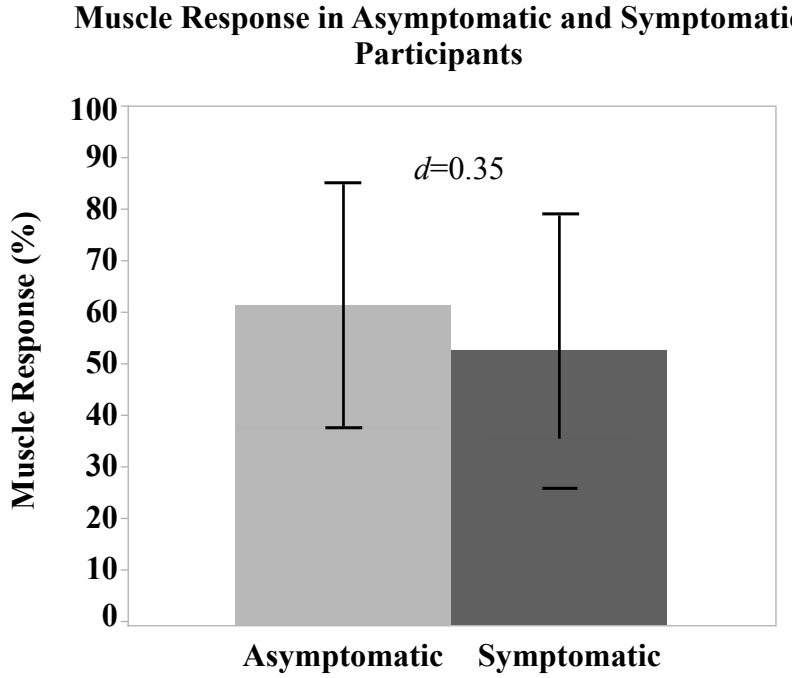

Figure 8.1. Percentage of muscle responses for each pain group across all EMG recording locations. A trend of greater muscle responses in the asymptomatic group and a small effect size of pain was present.

Greater muscle responses occurred in the muscles recorded with the multifidus electrodes than the superficial electrodes (β=4.3%, SE=1.9%, p=<0.01), and greater muscle response occurred during the L3 manipulation than the SI manipulation (β=5.3%, SE=2.2%, p=0.02). In the multifidus electrodes a small effect size of pain was present during the SI manipulation (d=0.23). In the superficial electrodes a small effect size of pain was present during the L3 and SI manipulations (0.49 and 0.38 respectively) (fig. 8.2).

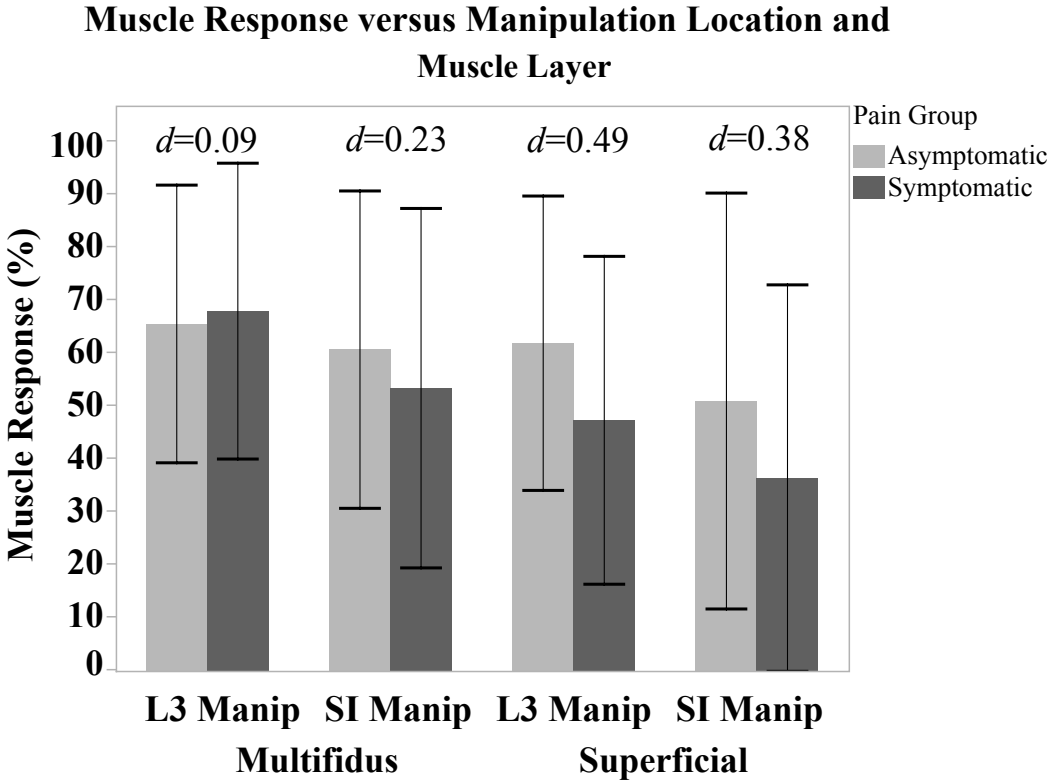

Figure 8.2. Muscle response for each pain group (asymptomatic, symptomatic) for the L3 and SI manipulation locations and the multifidus and superficial electrodes. A trend of greater muscle responses in the asymptomatic group with small effect sizes of pain were present.

8.3.2 Muscle activity onset delays

Muscle activity onset delays (when activity occurred) ranged from 0 to 395msec for the asymptomatic participants and from 1 to 397msec for the symptomatic participants. The mean onset delay across all active muscles in symptomatic group was 14msec longer than the asymptomatic group. No effect size was detectable (d=0.14) and the difference was not statistically significant (β=4.7msec, SE=10.1msec, p=0.64) (fig. 8.3)

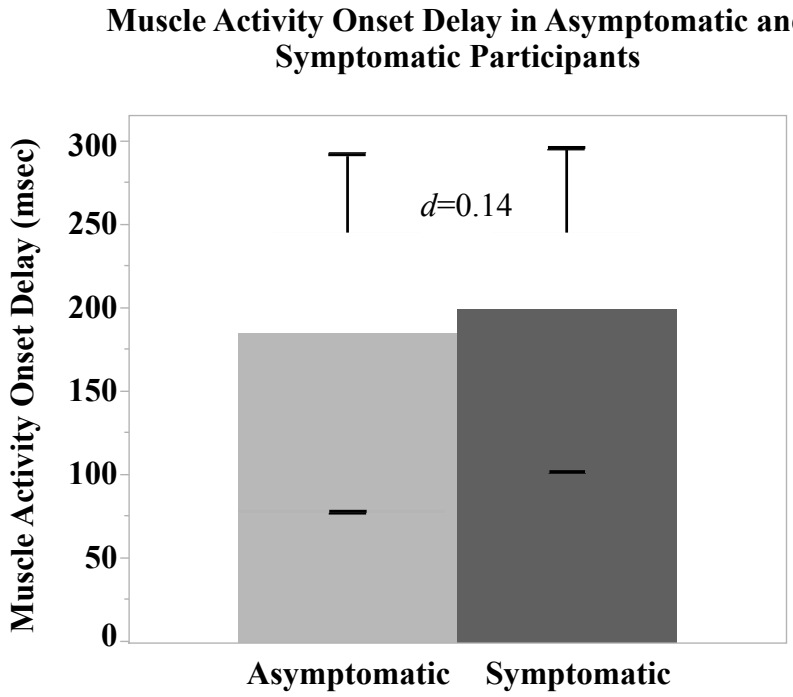

Figure 8.3. Muscle activity onset delays for asymptomatic and symptomatic participants across all EMG recording sites. A trend of longer delays in the symptomatic group was present with no detectable effect size of pain.

Muscle activity onset delay was longer for the symptomatic group in every EMG location except the right side multifidus L5 electrode, and a small effect size of pain was present at the left L2, quadratus lumborum and trapezius superficial electrodes (d=0.31, 0.29, and 0.27 respectively, fig. 8.4). Muscle activity onset delays demonstrated observably large variability across participants regardless of pain group.

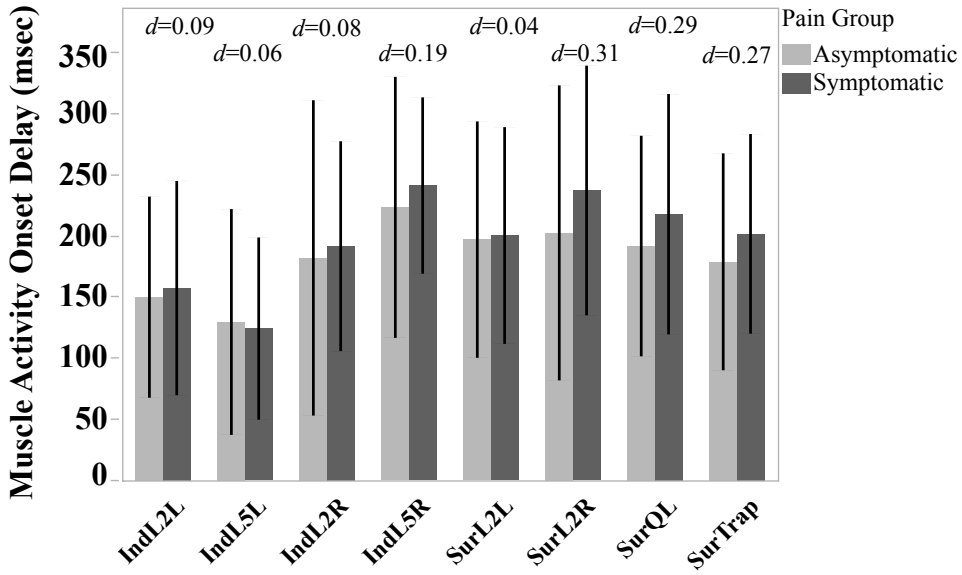

Figure 8.4. Muscle activity onset delays for all eight EMG locations for symptomatic and asymptomatic participants. A trend of longer onset delays was seen for the symptomatic group with a small effect size of pain group in three of the superficial electrodes.

8.3.3 Manipulation Order

A linear mixed model regression analysis revealed no effect of manipulation order on muscle response (β=0.3%, SE=0.86%, p=0.97) or muscle activity onset delays (β=6.0msec, SE=8.6msec, p=0.49).

8.4 Discussion

This investigation was the first to quantify differences in the muscle response and muscle activity onset delay between healthy participants (aymptomatic) and participants in pain (symptomatic) *during* a side-lying lumbar manipulation. Symptomatic

participants had less muscle responses and longer muscle activity onset delays than the asymptomatic participants. These differences suggest that underlying mechanisms of SM are linked to neuromuscular responses, and create a foundation on which to improve clinical delivery of SM based on quantifiable neuromuscular response variables.

Several limitations in this investigation should be considered. First, the treatment location in the symptomatic group was not chosen based on patient-specific assessment of clinical lesion or injury. The nonspecific application of SM allows an unbiased comparison of treatment locations across groups, but may not represent the response that would occur in clinical practice. Second, the state of the muscle (i.e. hypertonicity) may affect the presence or absence of muscle response (Lehman & McGill 2001), and was not quantified. Therefore, the results are generalizable only to the presence or absence of low back pain, and not to a specific clinical lesion. Last, the manipulations analyzed in this investigation were part of a larger data set that included two grade IV mobilizations applied to the L3 and SI spinal levels. To eliminate bias, treatment order was randomized, and an effect of treatment order on these muscle activity variables was not present according to the statistical analyses.

The longer muscle activity onset delay in the symptomatic group may indicate that patients in pain experience more excitability in capsular reflex pathways than muscle spindle pathways. The model predicted difference in delay was small (5msec) but potentially relevant given that previous work demonstrated muscle activity onset delays in the range of 2.4-18.2 msec (Keller et al. 2003) and that a spinal reflex is thought to occur within 120 msec (Wilder et al. 1996). Herzog (2000) proposed that two different

pathways – muscle spindle pathway and capsule mechanoreceptor pathway – are involved in the response to SM, and are likely differentiated by time delay. In addition, Herzog (2000) anticipated that muscle spindle pathways would be activated before mechanoreceptor pathways due to the reliance of large diameter IA tracts, and may characterize the response in our symptomatic patients.

Quantifying the similarities and differences in the neuromuscular response between asymptomatic and symptomatic participants provides insight into how SM achieves a therapeutic effect. Overall, symptomatic participants demonstrated a similar neuromuscular response to asymptomatic participants, which indicates that as a population they may be studied in a similar manner to an asymptomatic population. The trends of greater muscle response and shorter muscle activity onset delays in the asymptomatic population could be used as a clinical indicator of an asymptomatic "status", and the goal of treatment for patients that visit the clinic. The most apparent effects of pain occurred in neuromuscular responses in muscles that were located farthest from the manipulation site (quadratus lumborum and lower trapezius) and recorded with superficial electrodes (fig. 2, fig.4). This may indicate that these muscles were primary generators of the participant's symptomatic condition. If SM can be used to influence the neuromuscular reflex pathways (e.g. muscle spindle pathway in a symptomatic patient), then the greater number of muscle activity responses and shorter delays in the symptomatic participants suggest activation criteria for an effective application of SM.

The large variability of our data supports the view that many factors other than pain influence the neuromuscular response to SM. Numerous low back pain generators

and etiologies such as muscular, arthrogenic, neurological, and discogenic exist that may contribute to differences in neuromuscular responses. In addition, no single treatment method may produce consistent responses across all forms of low back pain. As a result, design of future investigations on SM on neuromuscular response should optimize the study scope with the goal of detecting small differences with highly variable responses and accounting for other factors that may contribute to the neuromuscular response of participants in pain. Biomechanical investigations such as this one are often performed on a limited number of participants due to the significant collection and processing time required for this type of data. While our investigation was ambitious in its attempts to quantify the differences between these populations (40 participants), the variability in the data prevented strong statistical conclusions.

8.5 Conclusion

This investigation is the first to quantify and compare differences in the neuromuscular response during manipulation in symptomatic patients and asymptomatic participants. The results revealed trends that indicate that patients with low back pain have a lower rate of muscle response, and when muscle response is present they occur with longer onset delays following the onset of a treatment impulse. Differences in the presence and timing of neuromuscular response to SM between groups provides information and suggest which muscles and spinal pathways may be affected by the presence of pain. We anticipate that future work will build on this foundation to identify

specific mechanistic associations of SM with pain relief, and develop clinical indicators of effective delivery of SM.

CHAPTER 9: THE NEUROMUSCULAR RESPONSE TO SPINAL MANIPULATION IN ACUTE AND CHRONIC PAIN

9.1 Introduction

Low back pain is a well-documented health problem, with 30% of the US population experiencing LBP at any given time (Andersson 1999). Due to its complex etiology, parameterizing low back pain patients into subclasses is difficult with any degree of homogeneity (Malliou et al. 2006). There is lack of consensus on the subclassification of chronic low back pain (Andersson 1999), resulting in a wide range of prevalence estimates in the literature. The International Association for the Study of Pain defines chronic pain as any pain that lasts longer than 3 months (Bogduk 1994; Bogduk 1999) and low back pain that last for less than 3 months is considered acute (Parthan et al. 2006). Approximately 5-10% of low back pain sufferers go on to develop pain that lasts longer than 3 months. (Parthan et al. 2006). The lack of clear subgroup definitions presents challenges in study design when attempting to relate benefits of a specific treatment to subclasses of LBP patients.

SM is effective at reducing pain (Bigos 1994; Bronfort et al. 2004); however, mechanisms remain largely unknown (Herzog 2010) especially in subclasses of patients with low back pain. The inability to identify the subgroups of patients who are most likely to respond to SM contribute to the lack of clarity surrounding the efficacy of SM

(Flynn et al. 2002; Bronfort et al. 2004). Conflicting evidence exists on the effectiveness of SM in different patient populations: benefits have been shown in acute pain populations, but insufficient data to recommend it as a treatment for chronic pain (Shekelle et al. 1992).There have been few high quality trials to distinguish between chronic and acute patients and their response to SM, and future research that examines well-defined subgroups of patients has been recommended. A lack of clarity remains concerning the effectiveness of SM over other treatments and interventions (Assendelft et al. 2004). When prediction rules are used based on subclasses of patients, better outcomes for SM are achieved (Childs et al. 2004; Cleland et al. 2007). Controlled trials (MacDonald & Bell 1990) and clinical prediction rules (Childs et al. 2004) suggest that patients with more acute symptoms respond better to SM. A better mechanistic understanding of how SM affects these different classes of low back pain patients may clarify the inconsistent findings across studies and patients.

Spinal manipulation is thought to influence and mediate pain through neuromuscular mechanisms. Evidence-based models (Je Bialosky et al. 2009) identify manipulation as a biomechanical event that initiates a chain of neuromuscular responses, modulating pain through cord summation in the dorsal horn of the spinal cord. SM has been shown to have a favorable effect on increasing pain thresholds (Coronado et al. 2012). Stretching of the facet joint capsule and lumbar musculature including spindles occurs during SM (Cramer et al. 2006) resulting in changes in multifidus (MF) and erector spinae (ES) length and muscle spindle firing (Pickar & Wheeler 2001). Sensory input changes from tissues surrounding the spine affects reflex muscle responses (Cramer

et al. 2006) and pain sensitivity (Coronado et al. 2012). Participants with increased symptom frequency have shown a greater number of neuromuscular responses (Colloca & Keller 2001).

Postural control of the spine is based in part on the reaction time of the trunk muscles, including the multifidus. To maintain spinal stability during motions that cause intervertebral displacement a reactive muscular response occurs (Panjabi et al. 1989). MF timing differences have been reported in participants with LBP (Hodges & Richardson 1999; Hodges & Richardson 1996) and patients with chronic low back pain have demonstrated poorer postural control and longer muscle response delays than healthy controls (Radebold et al. 2001). Differences in multifidus activity have also been observed across pain subclasses with chronic low back pain patients having lower multifidus activity than healthy or acute pain patients during active exercises (Danneels et al. 2002). These differences were not observed in the lumbar erector spinae muscles.

Developing clinical prediction rules in tandem with the neuromuscular response will give clinicians insight into mechanistic changes that may be occurring with treatment progress. In the absence of quantitative data, clinicians use patient-centered outcomes to track the progress of low back pain patients. Clinical trials on SM have depended upon patient-perceived outcomes such as pain level and functional status (Bronfort et al. 2008; Lawrence et al. 2006) and are used in SM research largely because of a lack of other available outcomes (Goertz et al. 2012). The Oswestry Disability Index (ODI) is considered the most commonly used and valid instrument to evaluate the restriction of function in low back pain patients (Parthan et al. 2006) and has been used to chart

improvement with a manipulation to the SI joint (Flynn et al. 2002). The verbal rating scale (VRS) is a standard metric for quantifying subjective pain levels and has been used in SM studies (Cramer et al. 2013). The Baecke Physical Activity Questionnaire (BPAQ) has been used to evaluate the impact of pain on habitual physical activities (Vol et al. 2011). Combining outcome measures such as the VRS, ODI and BPAQ with quantitative muscle responses provides clinical insight into how different patient populations respond to SM.

The objective of this study was to investigate the connection of the neuromuscular response to SM to subclasses of low back pain patients by comparing the muscle responses and muscle activity onset delays in participants experiencing chronic and acute low back pain. Neuromuscular responses were associated with on self-reported pain level, disability, and activity level at the time. Our previous work identified factors including SM order and location, and response layer, location and side that may help improve study design in SM by identifying differences in subclasses of LBP participants. Identifying differences in the response of different subclasses of low back pain patients to SM may help improve clinical decision-making.

9.2 Methods

9.2.1 Participant information

Table 9.1. Mean ± SD participant anthropometric information.

	Acute Pain (n=20)	**Chronic Pain (n=20)**
Age (years)	30.0 ± 8.3	37.5 ± 11.1
Height (cm)	172.5 ± 9.7	168.2 ± 9.6
Weight (kg)	76.6 ± 13.9	71.1 ± 15.3
Pain Level	3.1 ± 0.7	3.3 ± 1.6

Forty participants between the ages of 18-55 with a history of low back pain during the previous four years visited the laboratory for one session lasting three hours in which lumbar muscle activity was collected during SM. Two groups of twenty participants were recruited – chronic and acute (table 9.1). The acute pain group was defined as having episodes of pain lasting less than three months (but within the last four years) and were required to be in pain (greater than two out of ten on a verbal scale) on the day of testing. The chronic pain group was defined as having one or more episodes of low back pain lasting longer than three months in the last 24 months and answered in the affirmative to three out of five disability questions. Chronic pain participants were not required to be in pain at the time of testing. Each group had an equal number of males and females.

Each participant was screened for contraindications to SM by performing an orthopedic and neurologic examination. Participants were excluded from the investigation if: their current level of pain exceeded a seven out of ten on a verbal pain

scale; they experienced radicular pain below the knee during orthopedic testing; or neurologic exam revealed absent reflexes, decreased sensation or weakness below the knee. Each participant provided written, informed consent in accordance with the institutional review board prior to the start of the experimental session.

9.2.2 Self-Reported pain questionnaires

Participants rated their pain using a verbal rating scale (VRS) on a scale from 0 to 10. They completed the Oswestry disability index (ODI) to assesss their level of disability and the Baecke Physical Activity Questionnaire to evaluate the effect of their pain on physical activities. The BPAQ produces three scores that are considered separately: 1) physical activity at work; 2) sport during leisure time; and 3) physical activity during leisure time excluding sport (see Appendix A.6 for questionnaire background).

9.2.3 Application of spinal manipulation

Two chiropractors, each with over ten years of clinical experience, performed high-velocity low amplitude (HVLA) SM at the L3 and Sacroiliac (SI) spinal level with a hypothenar contact in the side-lying position. The order of manipulations was randomized and the time between manipulations was between one and three minutes.

9.2.4 EMG and contact force instrumentation

Each participant was instrumented at eight different muscle sites (Figure 3.1). EMG locations included surface EMG over the right and left erector spinae at the L2 and L5 levels, the quadratus lumborum (QL) and the lower trapezius (Trap) on the left (superficial muscles). Indwelling recording sites (50mm, 25ga needle with a pair of 0.051mm, insulated, hooked wires and 200mm tail with 5mm bare-wire terminations) included the left and right multifidi at the L2 and L5 spinal levels and were inserted according to the protocol defined by Haig et al. (1991). A Noraxon TeleMyo DTS (Noraxon USA, Scottsdale AZ) system was used to record both surface and indwelling EMG signals. The thrust force from the contact hand was estimated using an optimized algorithm that combines measurements from a force plate (Bertec Corporation, Columbus, OH) embedded in the treatment table and force transducers attached to the practitioner while maintaining natural contact between the practitioner and the participant [Myers et al., 2012].

9.2.5 EMG signal processing

The raw EMG signals were sampled at 2000 Hz, bandpass filtered to remove movement artifact and high frequency noise (4th order Butterworth, 15-350Hz), and transformed using the TKEO (Li et al. 2007; Solnik et al. 2008) (equation 3.1)

9.2.6 Muscle responses and muscle activity onset delays

The presence or absence of a muscle response was determined using a double-threshold method containing both amplitude and duration components, specifically optimized for HLVA spinal manipulations (see Chapter 4). The muscle response variable was calculated by dividing the number of muscle locations with a response that met the threshold criteria, by the number of muscle locations evaluated, expressed as a percentage. Onset delay between the manipulation impulse and muscle activation was quantified as the time delay between the positive slope of the contact force and the first EMG activity that qualified as a muscle response.

9.2.7 Statistical analysis

To assess the self-reported pain and disability in the subclasses, differences in the VRS and ODI scores between the acute group and chronic groups were calculated using one-way between-groups ANOVAs. To assess the degree to which clinical outcome measures relate to the neuromuscular response, correlations between the ODI, VRS, and BPAQ scores and the muscle response and muscle activity onset delays were calculated using Pearson's correlation coefficient.

Differences in the muscle response and the muscle activity onset delay between the two muscle layers (multifidus and superficial), two manipulation locations (L3 and SI), manipulation side (left or right), manipulation order (first or second manipulation), and pain groups (acute and chronic) were compared using mixed linear regressions with a random effect for subject. Level of significance for all statistical tests was set at α=0.05.

Effect sizes for all comparisons were calculated using Cohen's *d*. A small effect was defined as $0.2<d\leq0.5$, a moderate effect as $0.51\leq d\leq0.79$, and a large effect as $d\geq0.8$.

9.3 Results

9.3.1 Description of acute pain and chronic pain participants.

One hundred sixty seven participants were screened and 60 participants met the criteria for inclusion. Twenty participants had no history of low back pain and were not used in this analysis. Twenty participants met the criteria for acute pain and 20 participants met the criteria for chronic pain (table 9.2).

Table 9.2. Mean ± SD participant self-reported pain and physical activity data.

	Acute Pain (n=20)	**Chronic Pain (n=20)**
Pain Level	3.1 ± 0.7	3.3 ± 1.6
BPAQ Work Index	2.3 ± 0.7	2.6 ± 0.7
BPAQ Sport Index	2.7 ± 0.8	2.6 ± 0.8
BPAQ Leisure Index	2.9 ± 0.5	3.0 ± 0.6

9.3.2 *Disability Scores*

A weak positive correlation (r=0.39) was found between Oswestry scores and pain levels. No correlation was found between muscle response and pain levels (r=0.12), Oswestry scores (r=0.14), Work Index (r=0.00), Sport Index(r=-0.19) and Leisure Index(r=-0.28). No correlation was found between muscle activity onset delay and pain levels (r=0.09), Oswestry scores (r=0.03), Work Index(r=0.03), Sport Index(r=0.07) and Leisure Index(r=0.05). The chronic pain group had higher pain scores (F=4.25, p=0.039) and higher ODI scores (F=26.60, p=<0.0001) than the acute pain group.

9.3.3 Muscle responses

There was no difference in the muscle responses between the acute participants and the chronic participants (β=0.0%, SE=4.9%, p=1.0) where β is the model-predicted regression offset of the acute group on the chronic group, and a positive value indicates a greater rate of response and a negative value indicates a lower rate of response. There was no effect size of the pain group on the muscle response (d=0.00).

There was no statistically significant difference between the first or second manipulation (β=1.9%, SE=1.8%, p=0.29) and no effect size of manipulation order on muscle response. There was no statistically significant difference in muscle response between the L3 and SI manipulation (β=2.8%, SE=1.7%, p=0.11) and no effect size of manipulation location. Across all subjects the multifidi response was 18.2% greater than the superficial muscles (β=9.1%, SE=1.7%, p=<0.0001) with a moderate effect size of muscle layer (d=0.54) (fig. 9.1). There was no statistical difference in the left or right-sided muscles in the muscle response (β=1.2%, SE=2.0%, p=0.53).

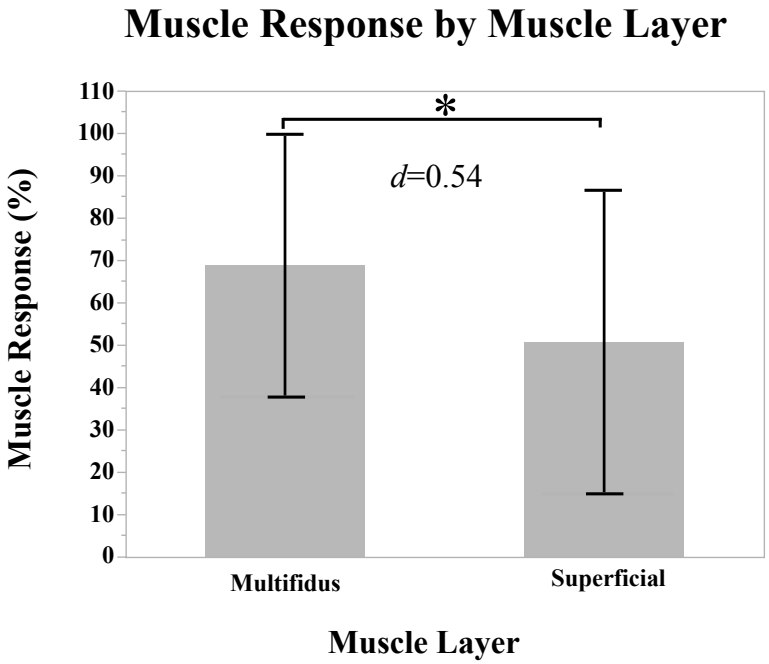

Figure 9.1. Muscle responses for multifidi and superficial muscle layers. More responses were observed in the multifidi. Star indicates a statistically significant difference.

9.3.4 Muscle activity onset delay

There was no statistically significant difference in the muscle activity onset delays between the acute participants and the chronic participants (β=5.5msec, SE=8.4msec, p=0.52) where β is the model-predicted regression offset of the acute group on the chronic group, a positive value indicates longer delays and a negative value indicates a shorter delay. There was no effect of the pain group on the muscle activity onset delay (d=0.14).

There was no statistically significant difference between the first or second manipulation (β=4.4msec, SE=8.4msec, p=0.59) and no effect size of manipulation order. There was no statistically significant difference between the pain groups in the L3

manipulation (β=-2.3msec, SE=7.0msec, p<0.73). In the SI manipulation, the acute pain group had longer onset delays than the chronic pain group (β=16.3msec, SE=6.0msec, p<0.008) with a small effect for pain group (d=0.40) (fig. 9.2).

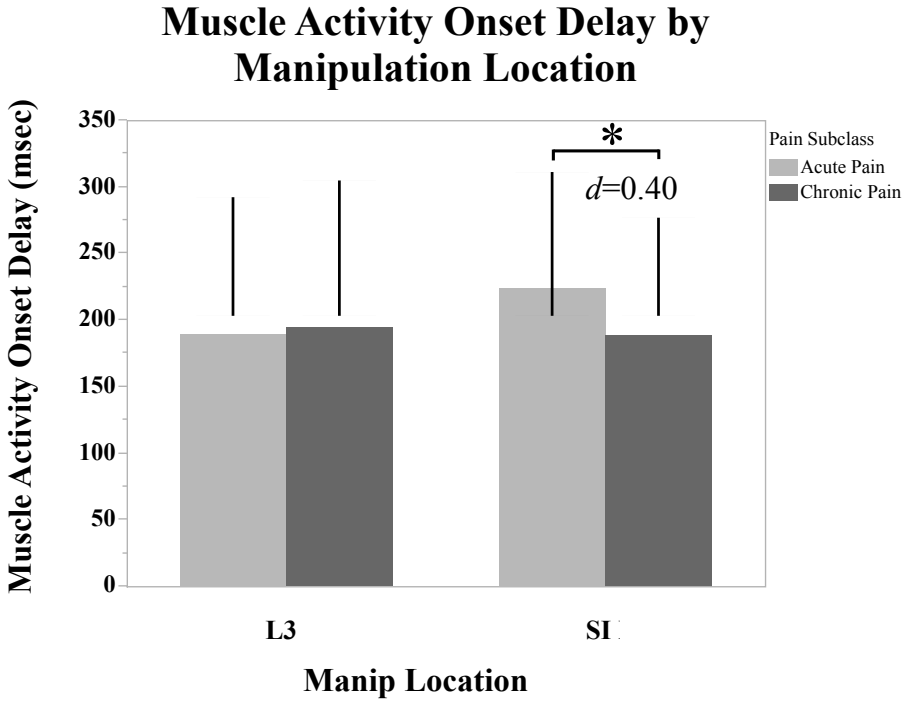

Figure 9.2. Muscle activity onset delays for the acute and chronic subclasses during the L3 and SI manipulations. Longer delays were seen in the acute pain subclass in the SI manipulation with a small effect size for pain subclass. Stars indicate a statistically significant difference.

There was no statistically significant difference between the pain groups in the multifidus (β=0.49msec, SE=8.5msec, p=0.95) or the superficial muscles (β=12.4msec, SE=10.54msec, p=0.25) but a small effect for the pain group (d=0.24) in the superficial muscles (fig. 9.3).

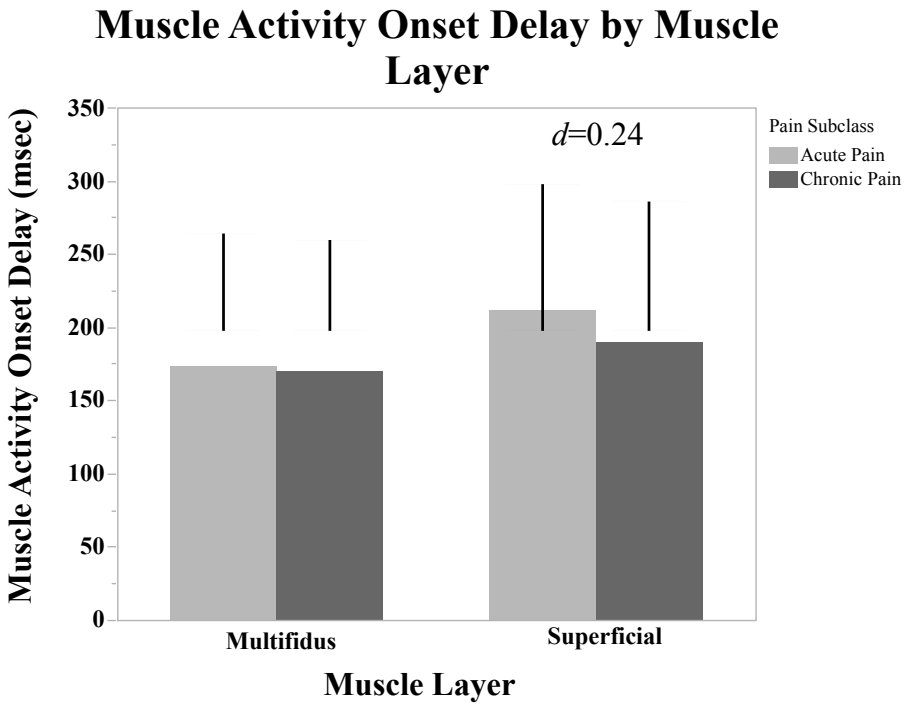

Figure 9.3. Muscle activity onset delays for the acute and chronic subclasses in the multifidi and superficial muscles. A small effect size for pain subclass was seen in the superficial muscles.

The left multifidus at L2 had shorter mean delays (β=-28.4msec, SE=9.59msec, p=0.003), the left multifidus at L5 had shorter mean delays (β=-63.1msec, SE=9.51msec, p<0.0001), and the right erector spinae at L2 had longer mean delays (β=39.0msec, SE=10.1msec, p<0.001). Small effects of the pain group were found at the right L2 multifidus (d=0.32), the left L5 multifidus (d=0.32), the right L5 multifidus (d=0.20), the left L2 erector spinae (d=0.32), and the QL (d=0.38) (fig. 9.4).

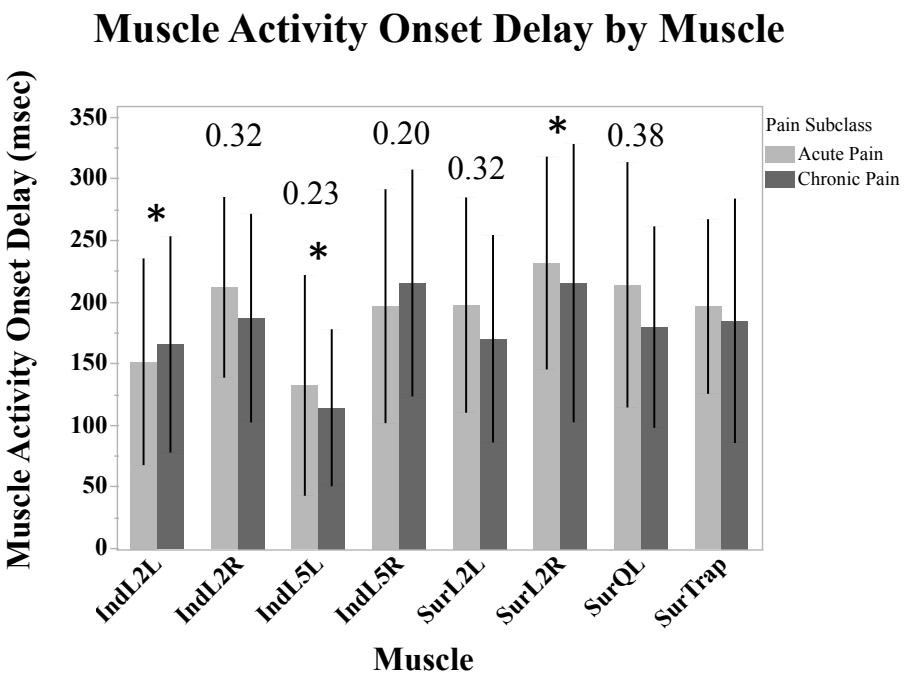

Figure 9.4. Muscle activity onset delays for the acute and chronic subclasses in all muscle locations. Stars indicate muscles that are statistically different from the model predicted mean. Pain group effect sizes are noted when at least a small effect size was observed.

The muscles on the left side had shorter delays than the muscles on the right (β=-28.9msec SE=4.36msec, p<0.001) with a moderate effect size for the side of the muscle (d=0.64) figure. There was no difference between the pain groups in the muscles on the left (β=3.6msec SE=9.37msec, p<0.70) or muscles on the right (β=6.37msec, SE=13.34msec, p<0.70).

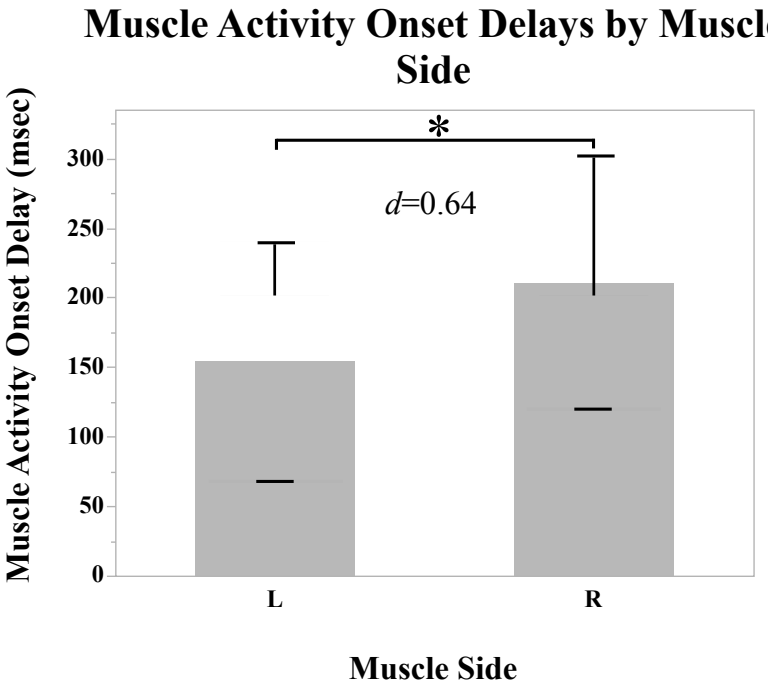

Figure 9.5. Muscle activity onset delays for the muscles on the left and right sides. Longer delays on the right side were observed. Star indicates a statistically significant difference.

9.4 Discussion

The goal of this study was to quantify differences in the muscle responses and muscle activity onset delays in acute and chronic low back pain participants. The results indicate that the neuromuscular response to SM in participants in pain is dominated by the multifidus and is consistent with passive movements as opposed to active movements that are dominated by the erector spinae. SM may mediate pain through influence on the afferent activity of the muscle spindles and central nervous system with the spindles of the multifidi providing more pain-gating input to the central nervous system. Compared

to acute participants, chronic participants had a greater tendency for shorter muscle activity onset delays consistent with a hyperactive state. These differences provide insight into how a mechanistic understanding of spinal manipulation informs the treatment of these potentially different populations.

In contrast to our previous work in healthy participants the difference in muscle responses between muscle layers becomes greater as pain and disability increase. The multifidi as a layer responded with a higher rate of response than the superficial muscles to SM, which suggests that the inclusion of the multifidi is essential to characterizing the complete neuromuscular response to SM. In a previous study using healthy participants (see Chapter 6) we found no statistical difference between the muscles in these two layers and previous work comparing healthy and LBP participants found similar increases in the response of the multifidi in LBP participants; however, the greater multifidi responses (4.3% model-predicted) found in this previous work was approximately half as much as the increase in multifidi responses (9.1% model-predicted) in the current study using acute and chronic pain participants. This greater multifidus response with increased chronicity of pain is contrary to the expectation that in patients with low back pain, a lower response might be observed because of the increase in muscle atrophy and fat infiltration seen in the deep MF compared to the superficial ES (Beneck & Kulig 2012).

To explain the findings in this study, a consideration for the type of activity being performed is informative. MF and ES activity during low-load stabilization type exercises - where the response of the muscles is passive - have shown no differences between muscle layers while higher load activities - where active voluntary recruitment is required

- have shown lower activity in the MF compared to ES in patients with LBP (Danneels et al. 2002). These results confirm the tendency of the MF to dominate the response of the low back musculature in passive and low-load activities as SM is considered a passive activity with reflexive muscle activity considered too fast to be voluntary (Herzog 2010). This is consistent with the theory that the MF is involved in segmental motion and stabilization while the ES considered a prime mover of the trunk (Macintosh & Bogduk 1986). SM results in a MF response that is more similar to low-load stability exercises than high-load active movements.

The neuromuscular responses observed in this study support a model of the mechanisms of SM that includes the mediation of pain through influence on the afferent activity of the muscle spindles and central nervous system (Je Bialosky et al. 2009); and add the quantification of these responses in different locations and pain groups. SM is thought to influence the central nervous system through sensory input from the muscle proprioceptors (Pickar & Wheeler 2001). By stimulating muscle spindle mechanoreceptors, SM acts as a "counter-irritant" stimulus, inhibiting dorsal horn cells involved in the transmission of nociceptive input (George et al. 2006). It is well established that the muscle activity of a skeletal muscle is positively related to the activity of its spindle afferents (Vallbo 1970; Dimitriou 2014) making the measurement of efferent EMG activity as performed in this study a proxy for the measurement of afferent activity. Based on this model, the increased muscle responses seen in the multifidi compared to the superficial muscles in this study indicate that in these painful

populations the multifidi spindles provided more pain-gating input to the central nervous system.

The finding of shorter muscle activity onset delays with greater chronicity can be explained in the context of the pain-spasm-pain model. In spite of a generally lower number of responses in the superficial muscles (ES, QL and Trap), these muscles tended to reveal differences between the chronic and acute pain subclasses more consistently than the deep muscle layer (MF), and indicates that muscle activity onset delays may be shorter as the chronicity of pain increases. It is possible then, that the presence of pain causes a delay in the response compared to healthy participants (Hodges & Richardson 1996), but these longer delays do not get progressively greater as the chronicity of pain increases. Instead, muscle activity onset delays appear to shorten as chronicity increases at least in the superficial muscles measured in this study. So while shorter muscle activity onset delays are considered advantageous for postural control of the lumbar spine (Radebold et al. 2001) and might not be expected to shorten as the chronicity of pain increased, the shorter delays observed in the superficial muscles in this study are consistent with pain models that postulate the pathologic hyperactivity of painful muscles (Roland 1986). These findings underscore the concept that muscular compensations for pain in the low back are complex, task-dependent, related to specific pathology, and highly variable within and across individuals (van Dieën et al. 2003).

The location that the spinal manipulation is delivered appears to play a role in muscle activity onset delay differences between the acute and chronic subclasses with faster responses observed in the chronic subclass during the SI manipulation that were

not seen when analyzing both manipulations together. The location of clinical pathology was not the focus of this investigation and was not measured in these participants. Given the close proximity of the manipulations and the corresponding lack of differences observed in our previous work in healthy participants, it is possible that the SI manipulation provided a treatment effect to the site of clinical pathology in some of these participants, resulting in differences in the onset delays between the pain groups. This finding is supported by the fact that the left-sided treatment used in this study resulted in shorter muscle activity onset delays than the right, pointing to an effect that is related to the location and side of the SM.

Quantifying the neuromuscular response to SM during physical activities and postural exercises designed to improve low back muscular function is an area for future exploration. To date, the timing of the neuromuscular response has not been a focus of manipulation literature. Evidence exists that during voluntary activities participants with pain have delayed muscle responses resulting in inefficient stabilization of the spine (Hodges & Richardson 1996) compared to healthy participants. The presence of SM's effect on the efferent neuromuscular response has implications for SM as a treatment for the muscular function of the spine. Because repetitive stimulation of these same pathways through exercise can improve muscle firing ratios (Ng et al. 2008), lead to faster postural reflexes (Marigold et al. 2005), and improve muscle onset latencies (Clark & Burden 2005) it is possible that the repetition of SM could have a similar effect.

Improvements in ODI scores have been used to demonstrate the validity of clinical prediction rules designed to identify those patients most likely to benefit from

spinal manipulation (Cleland et al. 2007). The ODI scores in this study had a mean score indicating a moderate disability, which is less disability than the scores from severely disabled participants used to establish the predictions rules. The chronic pain definitions used in this study resulted in the recruitment of a chronic group with higher levels of pain and disability than the acute group. The ODI and VRS scores for the participants in this study were similar to a previous SM study using a similar definition for chronic LBP (3 months) that also had greater scores as the chronicity of LBP increased (Colloca & Keller 2001).

The primary limitation of this study is that the SM was not directed at a clinical lesion such as a site of vertebral immobility, or a palpated hypertonic muscle. Previous studies have noted more consistent EMG amplitudes when the SM was directed at palpably taught muscles (DeVocht et al. 2005) and a review article suggested that the presence of a clinical lesion may influence the muscular response to manipulation (Lehman 2012). Knowing if and where a clinically relevant painful site existed would be useful in interpreting effects of the chronic pain group on the 8 muscles (Figure 4). The benefits of this study design, with its standardized manipulation sites, include the ability to directly compare manipulation locations and responses across subjects, which was considered of primary importance. Future work may consider the trends seen in this study and apply it to clinical lesions.

9.5 Conclusions

The neuromuscular response to SM in participants in pain is dominated by a response in the multifidus which is more similar to low-load stability exercises than high-load active movements. Chronic pain participants had a tendency of shorter muscle activity onset delays that were more evident in the superficial muscles during the SI manipulation. The neuromuscular responses seen in this study have implications for the delivery of SM as a treatment for the muscular function of the spine in these two subclasses of pain.

CHAPTER 10: SUMMARY AND CONCLUSIONS

A comprehensive data set of neuromuscular responses to SM in both healthy and LBP participants was generated for 60 participants by comparing onset delay detection methods, identifying treatment and response factors that affect the response in healthy participants, determining the effects of pain, and comparing responses across subclasses of participants in pain.

A comparison of two methods for muscle activity onset detection using EMG, the double-threshold method and the cross-correlation method, is presented that combines optimized contact force estimation with EMG recordings. The use of the double-threshold method with an 8 SD amplitude and a 10 msec duration threshold is recommended as the method that best represents the timing response to SM. The interpretation of muscle activity onset delays is critically dependent on the criteria used to determine both the onset of the force application and when a muscle is active, and should be reported in future studies on SM.

Two factors were identified that affect the neuromuscular response to SM in healthy participants: 1) *Treatment Factors* and 2) *Response Factors.* These results suggest that Treatment Factors such as manipulation order and location had little effect on the neuromuscular response; however, Response Factors including the responding

muscle location, layer and side revealed tendencies of lower response rates, and longer muscle activity onset delays as the distance from the manipulation location increased, and should be considered in future study designs.

Using the previously established methodology and with consideration for the Treatment and Response Factors observed in a healthy population, comparisons to participants in pain were performed. Symptomatic participants had less muscle responses and longer muscle activity onset delays than the asymptomatic participants indicating that patients in pain may experience more excitability in slower capsular reflex pathways than faster muscle spindle pathways compared to healthy participants.

Comparisons between two subclasses of participants in pain indicated that chronic participants had a greater tendency for shorter muscle activity onset delays than acute participants, consistent with a hyperactive muscle state. The neuromuscular response to SM in participants in pain is dominated by the multifidus and is consistent with passive movements as opposed to active movements that are dominated by superficial muscles. SM may mediate pain through influence on the afferent activity of the muscle spindles and central nervous system, with the spindles of the multifidi providing more pain-gating input to the central nervous system than superficial muscles.

The methodology developed, the factors identified, and the differences in participants in pain can be used in future work to further explore the mechanistic relationship of SM and muscle activity. First, the results of this study suggest that different pathways and muscles dominate the passive response to SM in participants in pain. Understanding how these pathways are affected during active rehabilitation

stability exercises, and voluntary movements such as sit-to-stand and lifting activities before and after SM will add to mechanistic understanding. Comparisons across healthy participants and participants in subclasses of pain will aide in developing clinical prediction rules for the application of SM. Second, the results of this study imply possible trends in the response patterns to SM. Future work can include identifying the timing response patterns during rehabilitation exercises and whether SM has an effect on these patterns in different pain subclasses. Finally, this work forms the foundation on which longitudinal studies can be performed, relating the clinical outcomes of SM to changes in neuromuscular response over time in subclasses of participants in pain. Future investigations on SM on neuromuscular response should optimize the study scope with the goal of detecting small differences with highly variable responses that may contribute to the neuromuscular response of participants in pain.

This investigation uses novel methods to improve upon previous applications, adds to the catalogue of muscle activation, and provides a basis for standardizing timing measures across investigations, gaining further insight into the neuromuscular effects of the spinal manipulation. As a result, the mechanistic understanding of the neuromuscular effect of SM in different subclasses of pain is improved.

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APPENDIX A: DATA PROCESSING METHODS

A.1 Kinematics and Kinetics

Practitioner kinematics and contact force direction were measured using a Vicon Motion Analysis system (Centennial, CO USA) sampled at 100Hz. Thirty-one reflective markers were placed on the practitioner during the manipulations, and an additional 12 markers were placed on the load cells during a static trial for reconstruction as virtual markers during each manipulation. Twenty-three markers were placed on the participant to record participant kinematics. Marker data was imported into MATLAB (Mathworks Inc, Natick MA) and digitally low-pass filtered (4^{th} order Butterworth) with a cut-off frequency of 20Hz

Kinetic data was collected via a force plate (Bertec Corporation, Columbus, OH) embedded in the treatment table to capture forces and moments during the manipulation. To capture kinetic data from the contact points, load cells were attached to the practitioner to record contact forces between the left hand of the practitioner and left shoulder of the participant, and the right thigh of the practitioner and left thigh of the patient (fig. 6.1). For each participant, four criterion standard trials were performed with a load cell in the practitioner's treating hand (right hand) for comparison to experimental trials when this load cell was removed to preserve normal treatment contact between the

practitioner's right hand and the participant's low back. Raw analog data from the force plate and load cells were imported into MATLAB and digitally low-passed filtered (4th order Butterworth) with a cut-off frequency of 20Hz.

A.2 Contact Force Optimization

A.2.1 Optimization

The force from the practitioner's treating hand (right hand) during experimental trials was estimated using an optimized algorithm that combined measurements from the instrumented treatment table and the load cells attached to the practitioner (C. Myers et al. 2012). A non-linear downhill simplex was used to optimize a participant-specific weighting matrix that accounted for the contribution of the forces and moments obtained from the force plate in the treatment table and the force transducers on the practitioner's thigh and left hand. The weighting matrix that produced the smallest error between the measured force during a training trial using the load cell on the practitioner's right hand and the predicted force, was used to estimate the practitioner's right hand contact force during each experimental trial when the load cell was not present. The mean absolute difference between the measured force and the predicted force was -3.6 ± 9.1 N with 95% limits of agreement of -21.9 to 14.7 N (C. Myers et al. 2012).

A.2.2 Isight workflow

Isight (Dessault Systèmes Simulia Corp, Providence, RI) processing was carried out to obtain the optimized weighting matrix for each of the four study trials – two HVLA manipulations and two mobilizations (fig. A.1). For each trial the force was predicted using the weighting matrix that best minimized the downhill simplex cost function(C. Myers et al. 2012). A total of 2000 iterations were used to determine each weighting matrix.

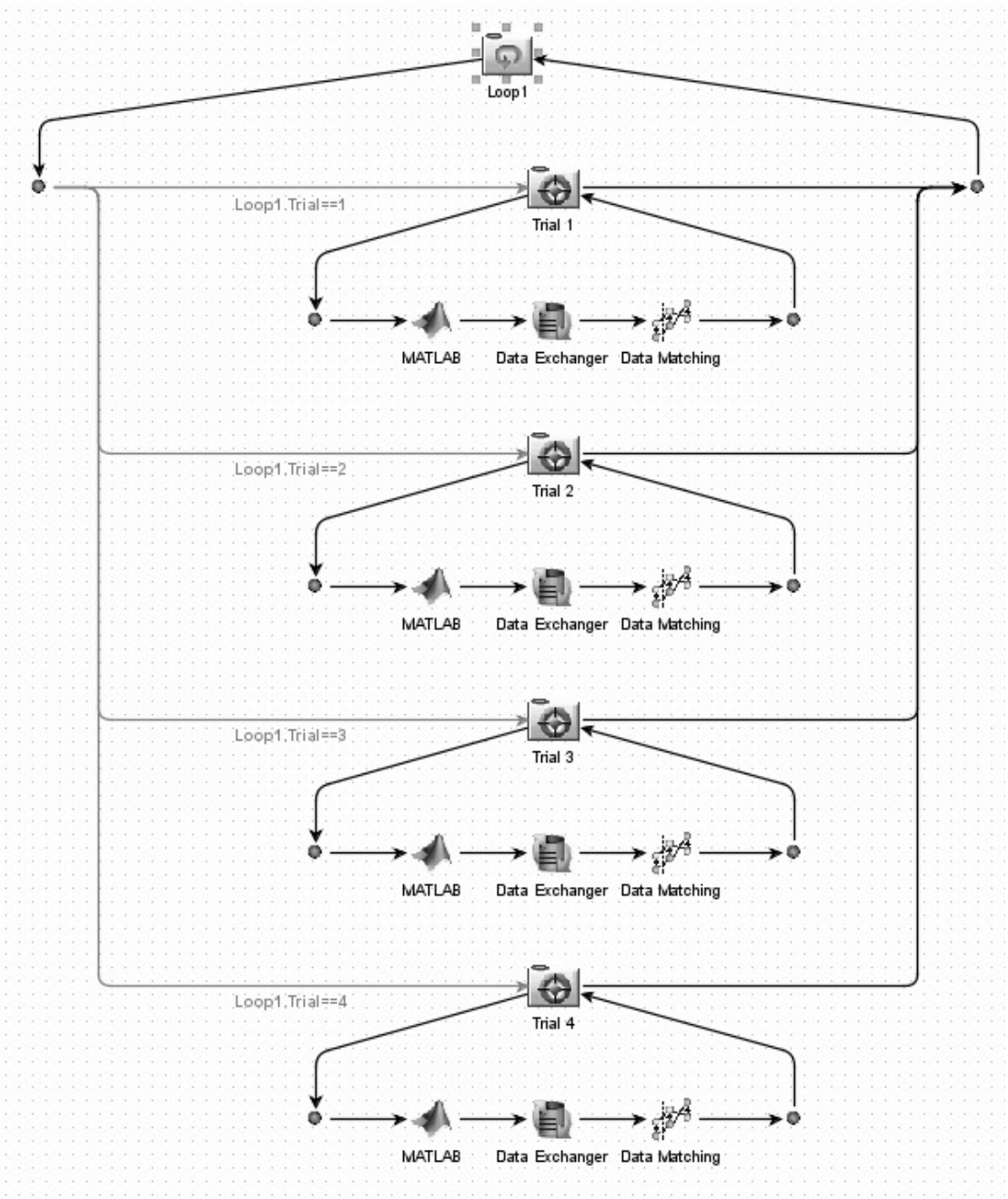

Figure A.1. Optimization workflow in Isight v. 5.7 Design Gateway. MATLAB was used to evaluate the cost function. The Data Exchanger converted the predicted force and the training force trial to a text file for use by the Data Matching function that used a weighted least squares approach to evaluate the difference between the training trials and the predicted trials.

A.3 EMG Processing

Raw EMG signals for all eight muscle sites were collected at 2000 Hz and band-pass filtered (4^{th} order Butterworth) between 15 and 350Hz. The TKEO (equation 3.1, fig. 3.1) was then applied to improve muscle activity onset detection. To create a linear envelope the TKEO-transformed data was full-wave rectified and smoothed using a low-pass filter with a cutoff frequency of 50Hz.

A.4 Muscle Activity Onset Delay Determination

After contact force prediction and EMG processing was complete, the muscle activity onset delay was calculated by plotting the EMG signal and the contact force signal together (fig. A.2). The amplitude threshold was calculated from 1 second of baseline data. Raw EMG data was plotted alongside the TKEO transformed data for visual verification of onset. Muscle activity onset delay was calculated as the difference between muscle activity onset and force onset. Only muscle activity that was contained in the first 400 msec following the onset of force was considered for analysis.

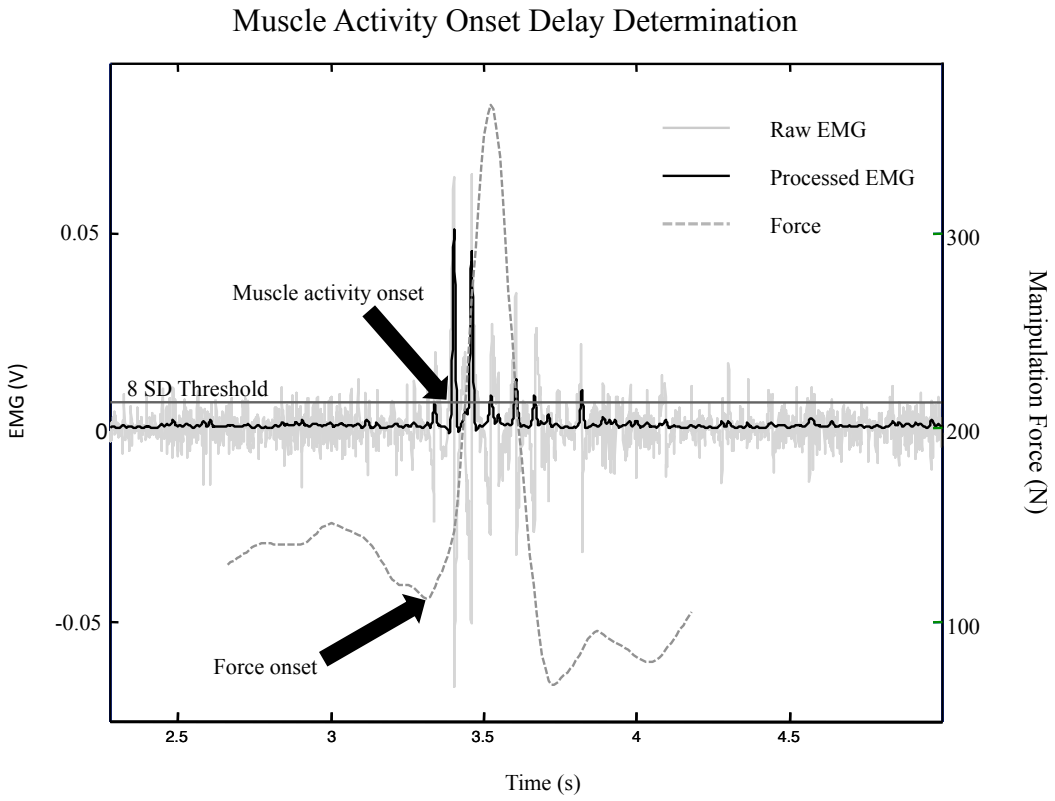

Figure A.2. Muscle activity onset delay determination. Onset of muscle activity was determined by the time at which processed EMG activity crossed the 8 SD amplitude threshold for 10 msec. Muscle activity onset delay was calculated as the time difference between muscle activity onset and force onset.

A.5 Statistical Methods

A.5.1 Mixed-model linear regressions

Linear regression is the examination of two variables that are linearly related or correlated (Portney & Watkins 2000). The present study design included repeated measures (multiple manipulations) in the same participants over similar areas and contained absent values for muscles that didn't respond. A mixed-model linear regression

with a random effect of subject was chosen to analyze differences between groups due to its advantages of dealing with missing values.

A.5.2 Effect size

Cohen's *d* effect size is defined as the difference between two means divided by the pooled standard deviation of the data set. It is a descriptive statistic that is not sensitive to the sample size. The interpretation of effect sizes is relative to the research situation and can be somewhat intuitive. Practical definitions of effects sizes have been published (Portney & Watkins 2000): a small effect size (≥ 0.2) is small enough to be imperceptible to the naked eye but not small enough to be considered minute; a medium effect size (> 0.5) is large enough to be visible to the naked eye; and a large effect size (≥ 0.8) represents a great degree of separation with very little overlap between populations. Conceptualizing the effect size can be done in terms of variance. The difference between two population means can be expressed as a percentage of one standard deviation. A small effect size therefore, implies the difference between the means is 20% of one standard deviation. Effect size comparisons were chosen for this study as an appropriate accompaniment to the inferential testing with mixed-model linear regressions.

A.6 Clinical Outcome Measures

Clinicians use questionnaires as objective outcome measures to determine if the treatment they are providing is effective and improving the patient's condition. Two

commonly used questionnaires are the Oswestry Disability Index (ODI) (Fairbank et al. 1980) and the Baecke Habitual Activity Questionnaire (BPAQ) (Baecke et al. 1982). A third, simpler metric is the verbal analog scale (VRS).

The ODI (also known as the Oswestry Low Back Pain Disability Questionnaire) is a commonly used questionnaire to measure progress in low back pain patients and is considered the gold standard in assessing low back pain (Fairbank & Pynsent 2000). It can be used to measure a patient's permanent functional disability and is one of the most commonly used patient-based outcome assessments in SM research (Khorsan et al. 2008). It has been used in the development of clinical prediction rules for SM (Flynn et al. 2002) and the comparisons of SM to other treatments for low back pain (Skargren et al. 1998; Giles & Müller 1999).

The BPAQ is a short questionnaire used to evaluate the impact of pain on habitual physical activities. The habitual physical activities are categorized as: 1) physical activity at work; 2) sport during leisure time; and 3) physical activity during leisure time excluding sport. The BPAQ has been shown to be a reliable measure in the evaluation of low back pain (Jacob et al. 2001) and can be used in epidemiological studies for analyzing the links between individual behaviors and health (Vol et al. 2011).

The VRS is used to assess global pain and asks patients to verbally rate the level of perceived pain intensity on a numerical scale from 0 to 10, with the zero representing "no pain" and ten representing "the worst pain possible". Verbal pain rating scales have been used in SM research to document improvement with manipulation over time and comparisons to non-manipulation control groups (Cramer et al. 2013).

To assess pain in studies of SM clinical trials have depended upon patient-perceived outcomes such as pain level and functional status (Bronfort et al. 2008; Lawrence et al. 2006). These have traditionally been considered qualitative by the scientific community and would benefit from correlation to more objective measures of the effects of SM. Patient-centered outcomes have been the primary focus of SM research largely because of a lack of other available outcomes (Goertz et al. 2012). Correlation of outcome measures including the VRS, the ODI and the BPAQ to the neuromuscular response to SM and different subclasses of low back pain provides a means of relating clinical measures of pain and disability to objective findings in the laboratory.

APPENDIX B: SUPPLEMENTARY FIGURES

This appendix contains data from all 60 participants used for analysis in this study, arranged by *Treatment Factors* and *Response Factors*, for the three subclasses of pain. Statistical comparisons across all three groups were not carried out as part of the scope of this study; however, charts are provided for comparison. All three subclasses of pain are included allowing the visualization of trends for muscle responses and muscle activity onset delays as the chronicity of low back pain increases from the asymptomatic group, to the acute pain group, to the chronic pain group.

B.1 Treatment Factors

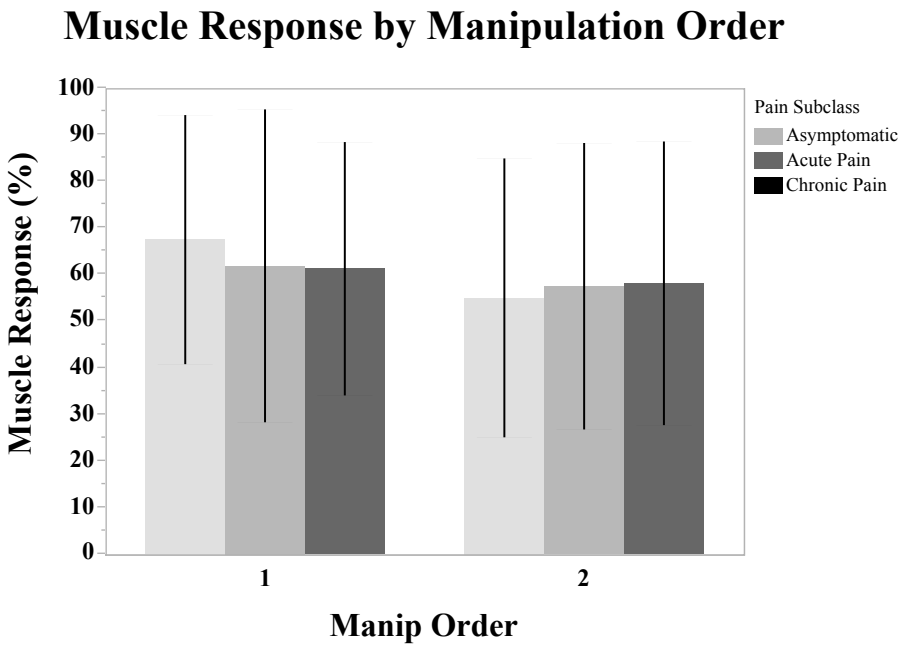

Figure B.1. Muscle responses by manipulation order for the three pain subclasses. Greater muscle responses are seen in the first manipulation compared to the second and the asymptomatic group in the first manipulation compared to both pain groups in the first manipulation.

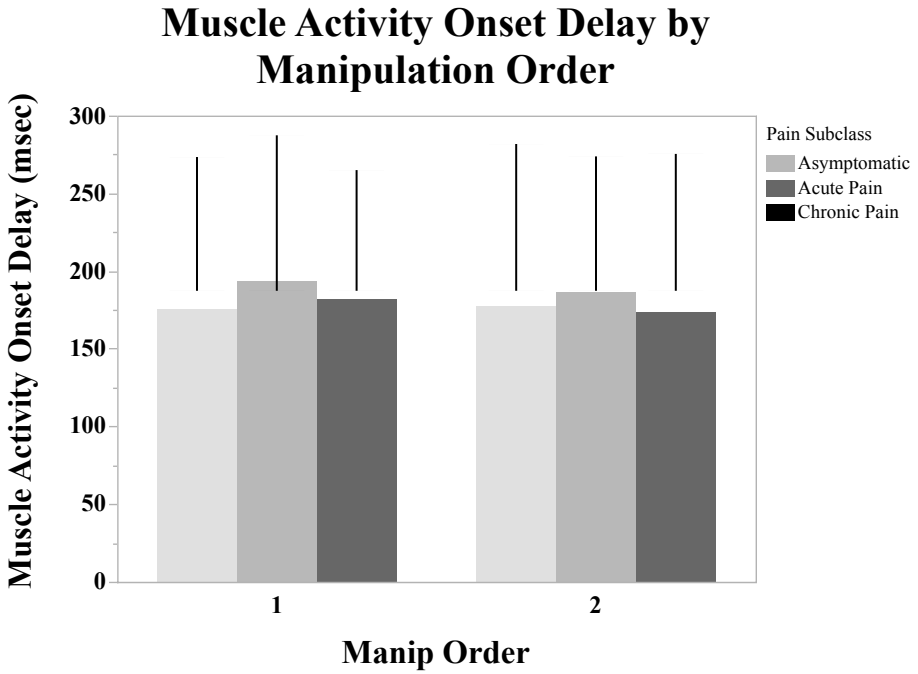

Figure B.2. Muscle activity onset delays by manipulation order for the three pain subclasses. Shorter onset delays are observed in the asymptomatic group compared to the acute pain group in both manipulations, and the chronic pain group demonstrates shorter onset delays than the acute pain group in both manipulations.

The greater number of muscle responses observed for the asymptomatic group may indicate that healthy muscles respond in greater numbers to SM than those experiencing pain. This trend is only seen during the first manipulation indicating this effect may not be present for subsequent manipulations. The trend of shorter muscle activity onset delays in the asymptomatic group may indicate healthy muscles respond faster in the first manipulation. As chronicity increases from acute to chronic shorter onset delays are observed consistent with the pain-spasm-pain model, which predicts hyperactivity of muscles in chronic pain. This same trend is not observed in the muscle responses.

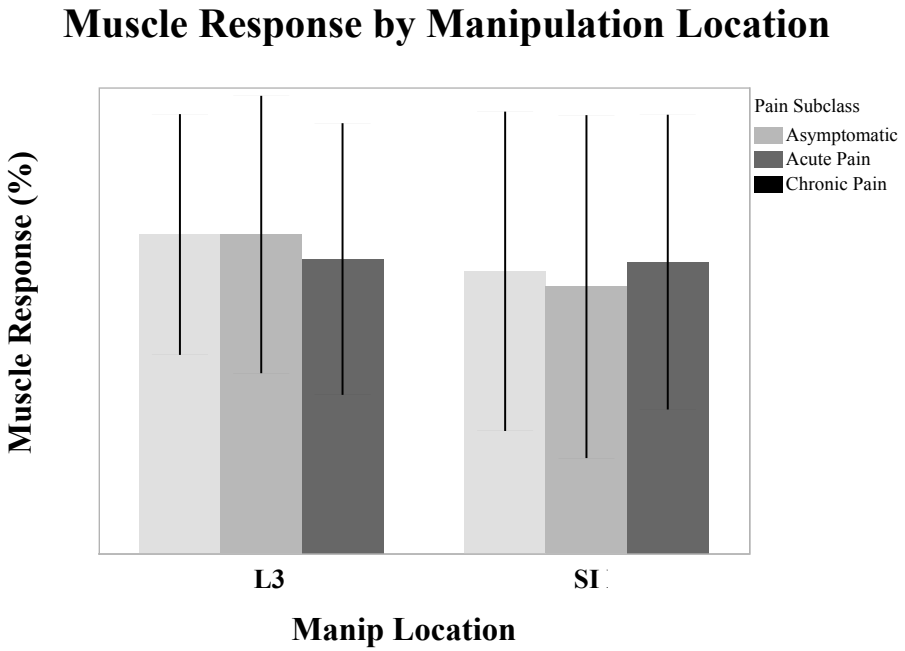

Figure B.3 Muscle responses by manipulation location for the three pain subclasses. A greater number of responses are observed in the L3 manipulation compared to the SI manipulation.

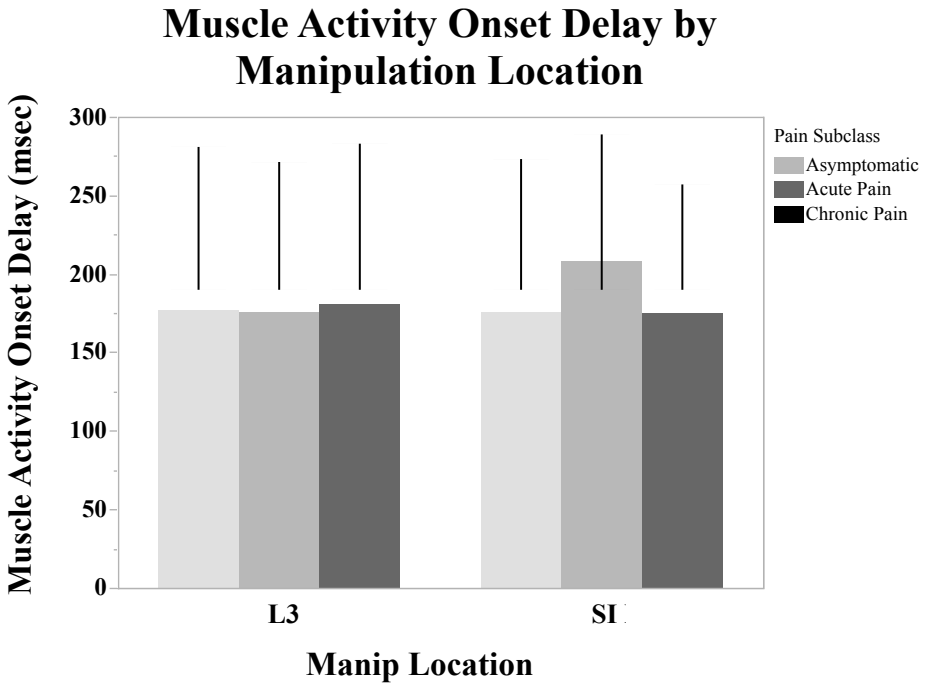

Figure B.4. Muscle activity onset delays by manipulation location for the three pain subclasses. Longer onset delays are observed in the acute pain group during the SI manipulation.

The measured muscles were closer in proximity to the L3 manipulation site than the SI manipulation site. The greater number of muscle responses observed in the L3 manipulation compared to the SI manipulation is consistent with the trend of increased muscle responses closer to the site of manipulation. The increase in muscle activity onset delays observed in the acute pain group during the SI manipulation may relate to the location of pathology or pain site in this group, which was not quantified in this study.

B.2 Response Factors

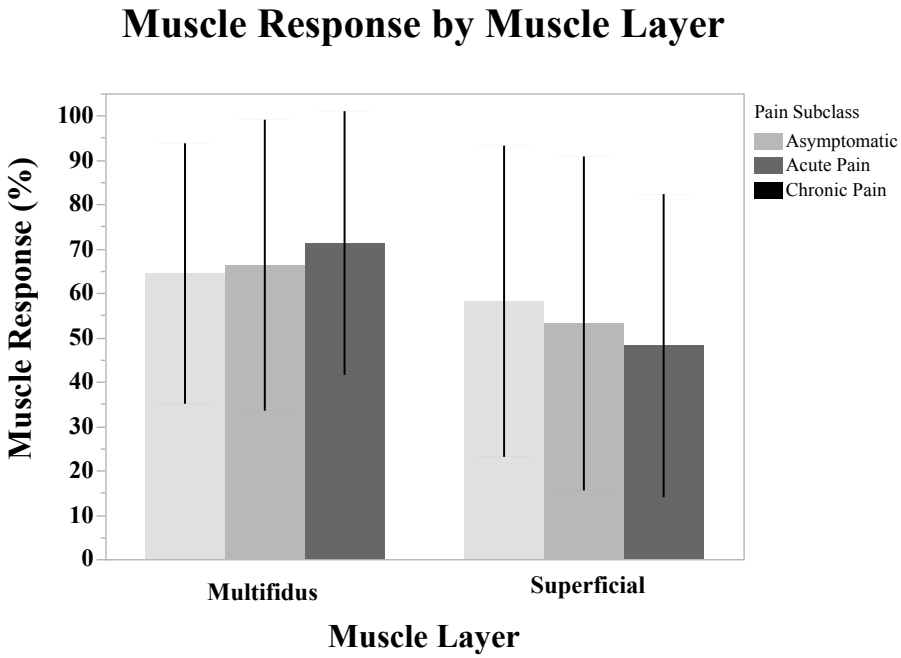

Figure B.5. Muscle responses by muscle layer for the three pain subclasses. Greater numbers of responses are seen in the multifidi compared to the superficial muscles. In the multifidi a trend of increasing responses is noted as the chronicity of low back pain increases, while this trend reverses in the superficial muscles.

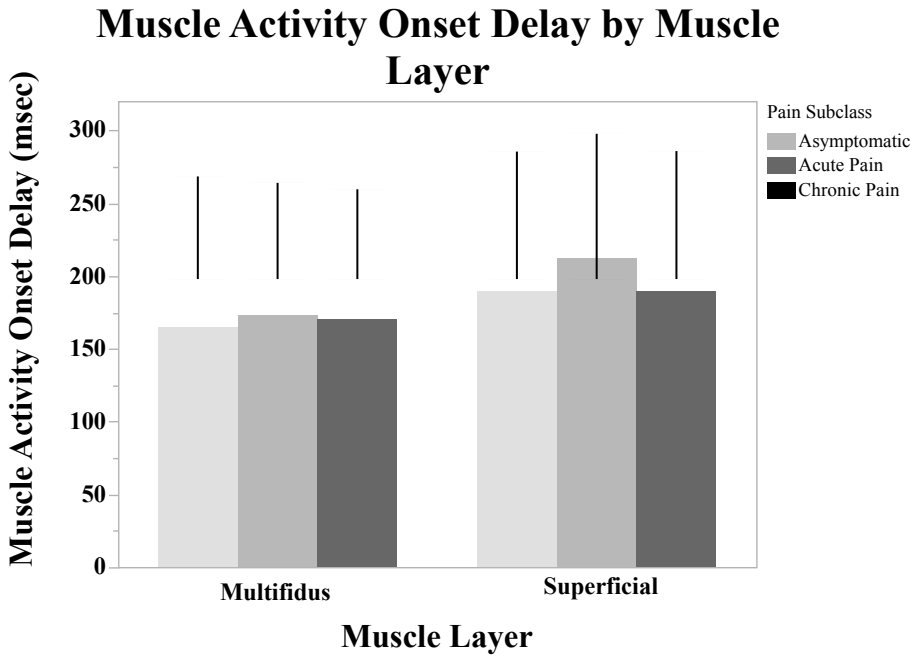

Figure B.6. Muscle activity onset delays by muscle layer for the three pain subclasses. Longer delays are observed in the superficial muscles compared to the multifidi.

The multifidi demonstrated a greater number of muscle responses with shorter onset delays across all three subclasses of pain, which is consistent with greater involvement of the multifidus seen in passive activities such as SM. As chronicity increased the multifidi response increased while the superficial muscle response decreased illustrating an inverse relation between multifidus and superficial muscle involvement during SM in participants in pain. As the chronicity of pain increases, it is possible that the multifidi (responsible for stability) are hyperactive consistent with the pain-spasm-pain model, while the superficial muscles (responsible for gross movements) are inhibited consistent with the pain-adaptation model.

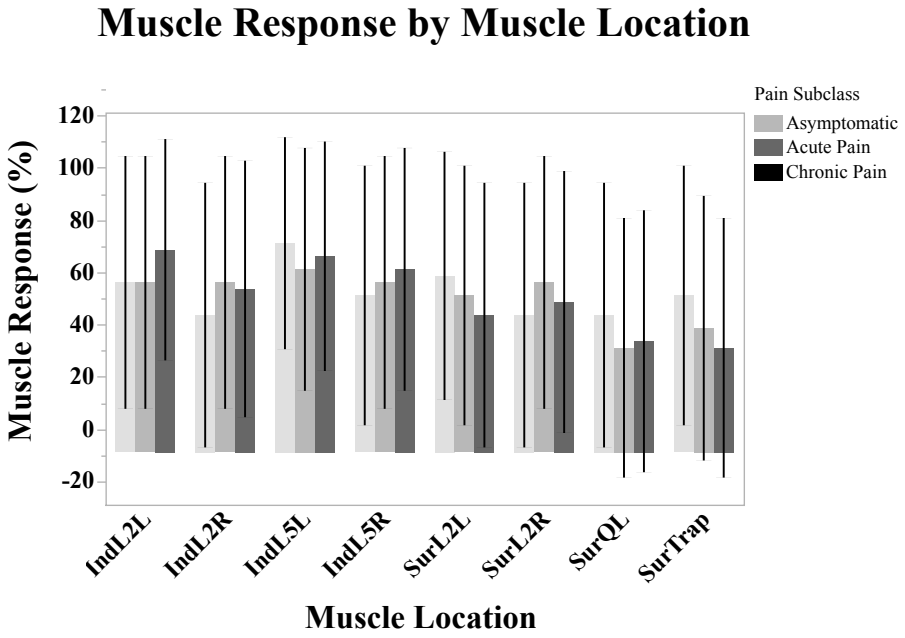

Figure B.7. Muscle responses by muscle location for the three pain subclasses. The 4 indwelling electrodes recording from the multifidi had a greater response than the surface electrodes recording from the superficial muscles. No clear trends across pain subclasses are noted.

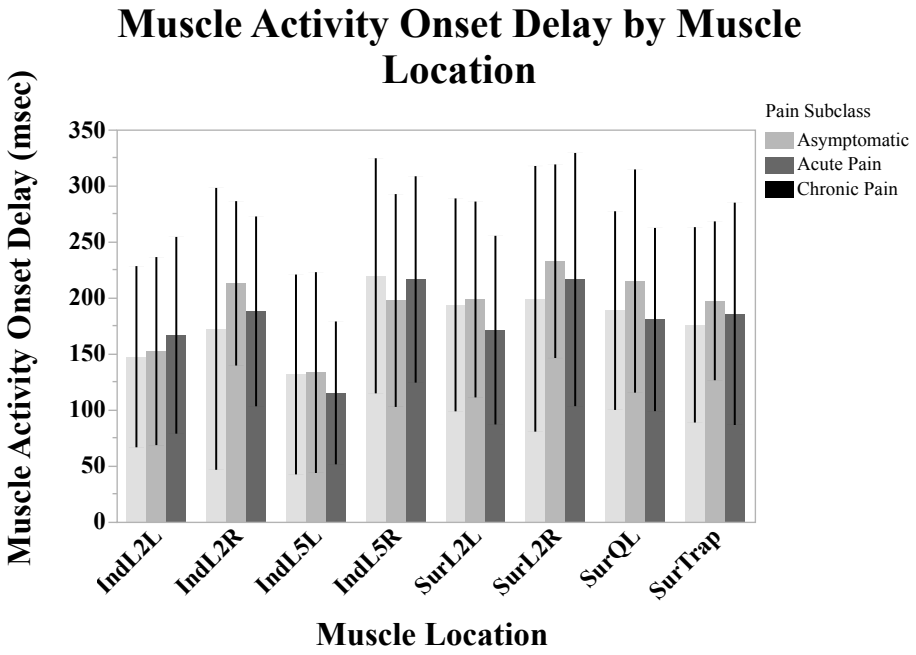

Figure B.8. Muscle activity onset delays by muscle location for the three pain subclasses. The 4 indwelling electrodes recording from the multifidi had a shorter muscle activity onset delays than the surface electrodes recording from the superficial muscles. No clear trends across pain subclasses are noted.

As the number of muscle sites considered increases, the number of observations in each group being considered decreases. The lack of clear trends across pain subclasses may result from the lack of statistical power that occurs when sorting the response by each muscle site.

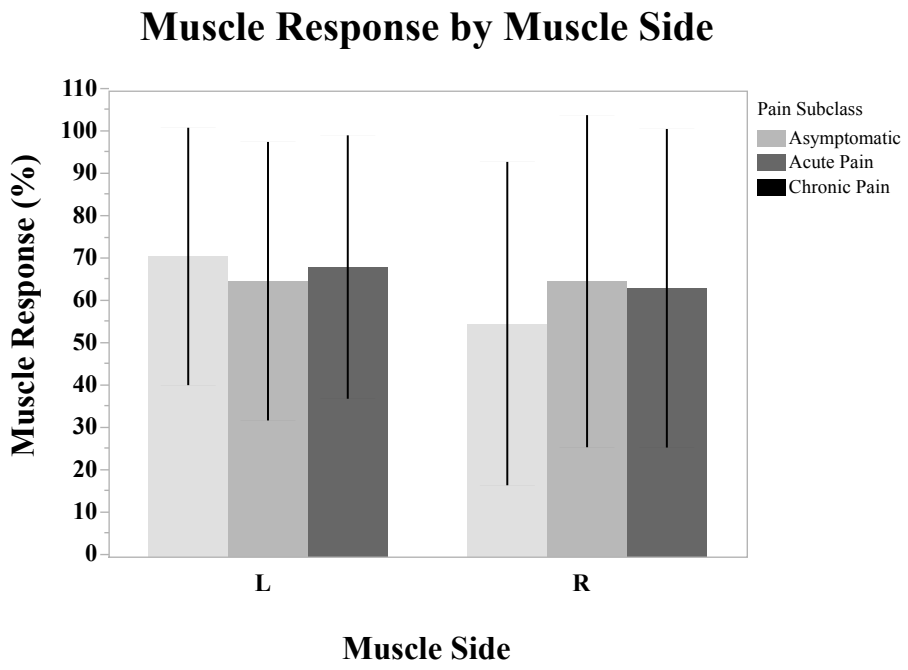

Figure B.9. Muscle responses by muscle side for the three pain subclasses. The muscles on the left side responded in greater numbers than those on the right side.

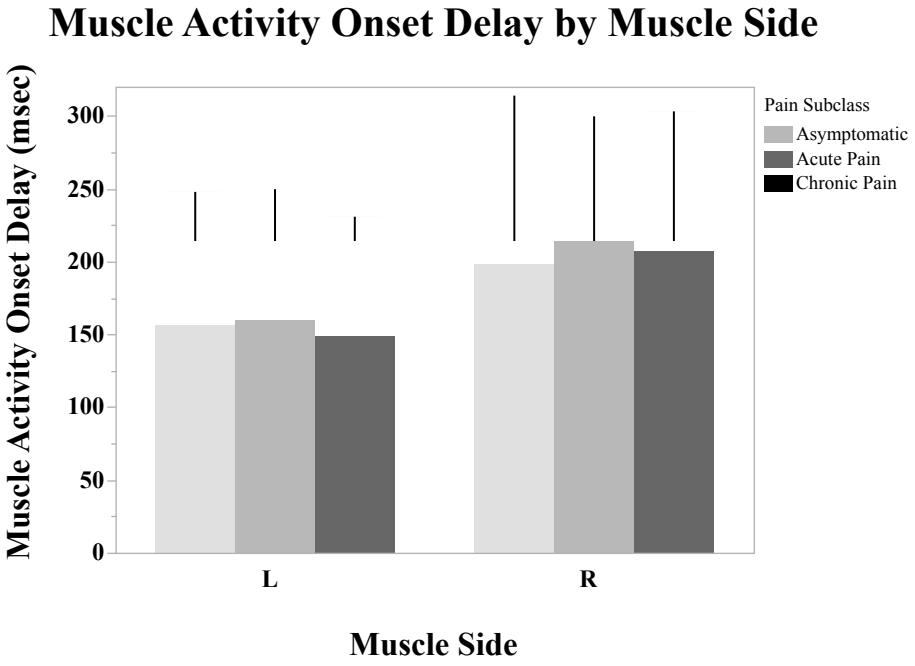

Figure B.10. Muscle activity onset delays by muscle side for the three pain subclasses. The muscles on the left side responded faster than those on the right side.

The muscles on the left side had a greater number of responses and responded faster than the muscles on the right side. No clear trends across pain subclasses were observed indicating that the side of the response may be more influenced by the manipulation location (all performed on the left in this study) than the chronicity of pain.

APPENDIX C: SUBJECT DATA

Table C.1. Mean ± SD participant anthropometric information.

	Male (n=30)	**Female (n=30)**
Age (years)	32.3 ± 11.5	34.3 ± 9.7
Height (cm)	177.1 ± 8.2	164.8 ± 6.2
Weight (kg)	79.9 ± 12.9	65.6 ± 11.0
Dominant Hand (right/left)	(27/3)	(26/4)

Table C.2. Mean ± SD participant self-reported pain, disability, and physical activity data.

	Asymptomatic (n=20)	**Acute Pain (n=20)**	**Chronic Pain (n=20)**
Pain Level	0	3.1 ± 0.7	3.3 ± 1.6
Oswestry Disability	N/A	20.5 ± 9.4	25.1 ± 12.7
BPAQ Work Index	2.4 ± 0.6	2.3 ± 0.7	2.6 ± 0.7
BPAQ Sport Index	3.1 ± 0.8	2.7 ± 0.8	2.6 ± 0.8
BPAQ Leisure Index	3.3 ± 0.7	2.9 ± 0.5	3.0 ± 0.6

APPENDIX D: CONFERENCE PRESENTATIONS AND PUBLICATIONS

Conference Presentations

Currie, Stuart J, Casey A Myers, Brian A Enebo, and Bradley S Davidson. 2012. "Anticipatory Activation of the Erector Spinae and Multifidus in Patients With and Without Low Back Pain." In *36th Annual Meeting of the American Society of Biomechanics*.

Currie, Stuart J, Casey A Myers, Brian A Enebo, and Bradley S Davidson. 2013. "Muscle Activation Onset Timing Recorded During HVLA Spinal Manipulation - A Methodological Comparison." In *Association of Chiropractic Colleges - Research Agenda Conference*.

Everitt, Alicia, Stuart J Currie, Brian A Enebo, and Bradley S Davidson. 2015. "Cavitation and the Neuromuscular Response to Spinal Manipulation." In *Association of Chiropractic Colleges - Research Agenda Conference*.

Currie, Stuart J, Alicia Everitt, Brian A Enebo, and Bradley S Davidson. 2015. "The Neuromuscular Response To Spinal Manipulation In The Presence Of Pain." In *Association of Chiropractic Colleges - Research Agenda Conference*.

Publications

Currie, Stuart J, Casey A Myers, A Krishnamurthy, Brian A Enebo, and Bradley S Davidson. 2015. "Methods of Muscle Activation Onset Timing Recorded During Spinal Manipulation." *Journal of Manipulative and Physiological Therapeutics*. *Accepted for publication.*

Currie, Stuart J, Casey A Myers, Catherine Durso, Brian A Enebo, and Bradley S Davidson. 2015. "The Neuromuscular Response to Spinal Manipulation in the Presence of Pain." *Journal of Manipulative and Physiological Therapeutics*. *Accepted for publication.*