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Neurophysiological Effects of Dry Needling to the Thoracolumbar Junction Multifidi in Subjects with Low Back Pain and Decreased Hamstring Length

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The Neurophysiological Effects of Dry Needling to the Thoracolumbar Junction Multifidi in Subjects with Low Back Pain and Decreased Hamstring Length

by

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A dissertation submitted in partial fulfillment of the requirements
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Nova Southeastern University
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Background and Purpose: Dry needling is becoming increasingly popular in the treatment of neuromusculoskeletal conditions. The neurophysiological effect of treatment, specifically those related to the sympathetic nervous system (SNS) is considered a relevant physiological mechanism contributing to a patient's rehabilitation. The primary purpose of this study was to investigate the neurophysiological effects of dry needling, as measured by sympathetic outflow and muscular flexibility. A secondary purpose of this study was to determine if changes in SNS activity correlate with clinically meaningful improvements in pain and disability. **Design:** This was a prospective, double-blind randomized clinical trial. **Subjects:** The study sample consisted of 54 consecutive volunteers recruited from outpatient orthopedic clinics in Montgomery County, Maryland, who presented with low back pain and decreased hamstring length in at least one hamstring. **Methods:** Subjects completed a demographic questionnaire, the Numeric Pain Rating Scale and the Oswestry Disability Index (ODI). Afterward, they underwent local and remote muscle length testing, as well as pressure pain threshold (PPT) testing. Subjects were randomly allocated to the treatment or placebo group. Measures of SNS activity were monitored and recorded before and after the treatment, and tests of muscle length and performance were re-assessed after treatment. Subjects returned 24 hours after their initial visit for muscle length testing, SNS testing, and to complete the Global Rating of Change, ODI, and Numeric Pain Rating Scale. **Statistical Analysis:** ANCOVAs were used for analysis of each variable of SNS activity as well as differences in local and remote flexibility. Differences between segmental and extra-segmental PPT changes were analyzed with a *t*-test. Pearson's *r* was used to determine if there was a relationship between immediate SNS outflow and clinically meaningful improvements. Alpha levels for all statistical tests were $p<.05$. **Results:** Electrodermal activity (EDA) differed between groups immediately post-treatment ($p=.002$), and all other measures of sympathetic outflow were not significant. Local flexibility was greater in the DN group immediately post-treatment ($p=.0495$). There were no segmental differences in PPT after DN, and measures of SNS outflow immediately post-treatment did not correlate with improvements in pain and disability. **Conclusion:** DN can potentially result in immediate changes in EDA and local flexibility.

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CHAPTER 1: INTRODUCTION

BACKGROUND

Dry needling (DN) is becoming more frequently performed by physical therapists (PTs) around the world to treat myofascial trigger points (MTrPs) and musculoskeletal pain.[1,2] In 2019, the American Physical Therapy Association issued a report that stated 35 states and the District of Columbia allow for DN by PTs, 8 states have not issued a clear position, and 7 states expressly prohibit DN by PTs.[3] DN is a form of trigger point therapy that evolved from using injections of local anesthetics directly into a MTrP to treat musculoskeletal dysfunction. Dr. Karel Lewit, a physician from the Czech Republic, coined the term "needle effect" when he found that hypoalgesia after penetrating a MTrP with a needle was completely independent of the substance that was being injected.[4] Although standard of care still dictates that the treatment of MTrPs is local injections of anesthetic, research has determined that there is no difference in outcomes between needling with and without an injectable substance.[4,5]

There is evidence that DN deactivates MTrPs, normalizes the chemical milieu to allow for proper function of acetylcholinesterase, releases muscle shortening, promotes self-healing of injured muscle, and decreases peripheral nerve sensitivity.[6] When the needle penetrates a muscle deep enough, it can facilitate a local twitch response (LTR) from a MTrP.[1] A LTR is a visible or palpable contraction of a muscle upon mechanical stimulation via needling or pressure to a sensitive site within a taut band of muscle.[7,8] DN is purportedly most effective when an LTR is elicited,[9] and this is one of the several ways in which DN differs from acupuncture.[10]

PROBLEM STATEMENTS AND GOALS

Although DN is being used more often in treatment of musculoskeletal disorders, there continues to be little agreement about the pathways on which it works. Research on the

neurophysiological effects of DN has increased in the past 10 years, however much about the treatment is still poorly understood. A better understanding of the neurophysiological mechanisms on which DN acts, and how it influences structures distant from the site of treatment, can lead to improved choices of therapeutic activities, and potentially superior outcomes.

Many studies have investigated the effects of joint mobilization or manipulation[11-21] on the sympathetic nervous system (SNS), but fewer studies have investigated the effects of DN.[22-24] Of the studies on joint mobilization, many have examined treatment to the cervical spine, specifically C5,[12,14-18] and tested SNS-related outcomes in the cervical spine, upper thoracic spine, and upper extremities (UEs).[5,11-15,17,18] Sampath et al[19] investigated neuroendocrine changes in healthy volunteers after manipulation to the thoracic spine, and included the lower extremity in their analysis. Their study showed no difference in blood flow to the calf muscle, as measured by near-infrared spectroscopy. Manipulation was performed at T5, and the lack of statistical significance may be because only the UEs receive direct sympathetic outflow from T5.[25] The sympathetic nerve fibers that supply the lower extremities (LEs) originate from T10 to L2,[26] and future research should investigate how DN affects the LE when its direct sympathetic connection is treated.

Zegarra-Parodi et al[21] performed a systematic review of the available literature on spinal manipulation and various measures of skin blood flow, as measured by skin temperature (ST), electrodermal activity (EDA) and pulse photoplethysmography (PPG), as an indicator of peripheral SNS activation and found that many of the published studies had small sample sizes and collected data on healthy, asymptomatic subjects. Some studies included in the systematic review showed increases in skin conductance and temperature, but others showed the inverse.

The authors concluded that these measure should be used in future studies along with clinical outcomes measures to explore which changes are clinically meaningful.[21]

Much of the available data on DN and muscle length come from studies with methodologies that examine a local effect, meaning the investigators measure only the length of the muscle that was treated.[5,27-29] Results of recent studies on the local effects of DN are mixed. There was no significant difference in muscle length in the LE after DN and sham DN to the LE,[27,28] however DN to the cervical spine did show improvement in muscle length greater than subjects who received no treatment.[29] While there is a limited number of studies on the local effects of DN on flexibility, there are fewer on the remote effects.[30] This dissertation study investigated both local and remote changes in flexibility.

At this time, there is minimal research on manual therapy treatment to the thoracolumbar (TL) spine and its effect on the LEs.[31] The thoracic spine is the origin of nearly all SNS outflow to the extremities, and should therefore not be overlooked as a potentially "silent" contributor to musculoskeletal dysfunction in the extremities.[32]

The goals of this dissertation study were:

1. To quantify the magnitude of the SNS response to DN at the TL junction in subjects with low back pain (LBP) and decreased hamstring length, using valid measures of SNS activity.
2. To describe the effect of DN at the TL junction on muscle length both local and remote to the site of treatment.
3. To determine if DN to the TL junction has a significantly greater segmental sympatho-excitatory effect than extra-segmental effect, as measured by pressure pain threshold (PPT) in the LE and UE.

4. To determine if immediate changes in SNS activity after DN are related to clinically meaningful outcomes at 24-hour follow-up.

RELEVANCE AND SIGNIFICANCE

SNS stimulation is capable of causing a profound effect on multiple body systems; there are approximately 20 postganglionic fibers (but can be as high as 200) to each preganglionic fiber from the spinal cord, and these postganglionic fibers can traverse many spinal segments before finally synapsing at the target organ or tissue.[31] One analysis in a systematic review showed manual therapy directed to the spine can increase heart rate by greater than 10% and respiration rate by 44%, suggestive of a multi-system response.[18]

SNS stimulation can result in hypoalgesia via the release of endogenous opiates. Endogenous opiates bind to receptors on afferent neurons and suppress neuronal activity to inhibit the transmission of nociceptive impulses.[8,33] They are also capable of suppressing descending impulses from the midbrain.[8] A greater SNS response may result in greater hypoalgesia, thus a patient may be better able to tolerate treatments or activities that were previously painful. This would be beneficial for patients with central sensitization, which is an increase in neuronal excitability within the central nervous system that decreases the threshold needed to elicit a painful response, and increases the area where one would perceive pain to beyond where there is inflammation.[34] The relief one feels after DN can be used as a "springboard" on which new movement patterns can be learned pain-free or with less muscle inhibition from dysfunctional motor units.[2,35]

The impact of DN on the SNS should be investigated, as it may provide a safer alternative for treatment of pain. Doctors prescribe opioid medications and nonsteroidal anti-inflammatory drugs (NSAIDs) to treat pain associated with central sensitization. Both

medications carry a substantially greater risk of adverse events (AEs) than DN.[36] Controlling pain has become a critical topic amidst the opioid crisis in the United States. Patients and health care provides may seek alternatives to prescription medications because of the AEs and possibility of addiction that can be associated with these medications. According to the National Institute on Drug Abuse, there was a 2.8-fold increase in the number of opioid-related deaths between 2002 and 2015.[37] The greatest increase in drug-related deaths occurred in opioids, with nearly 1/3 of all overdoses in 2016 being attributed to synthetic or semi-synthetic opioid medications.[37]

ELEMENTS

Research Questions

Research questions for this dissertation study were:

1. What are the differences in indicators of SNS activity, such as heart rate variability (HRV), EDA, and ST in the LE when DN or sham DN is performed at the TL junction in subjects with LBP and decreased hamstring length?

2. How does DN to the TL junction affect lumbar paraspinal and hamstring length in subjects with LBP and decreased hamstring length?

3. How far superiorly does the sympatho-excitatory response ascend when DN is performed at the TL junction in subjects with LBP and decreased hamstring length?

4. Do immediate changes in SNS activity correlate with greater clinical improvements at short-term follow-up, as measured by pain rating, global rating of change (GRC), and the Oswestry Disability Index (ODI)?

Hypotheses

Hypotheses for this study were:

H_1: DN will cause a greater SNS response than sham DN, as measured by HRV, ST, PPT, and EDA in the LE.

DN has been found to be superior to sham needling in many outcome variables, including but not limited to reducing pain,[38,39] improving self-reported function,[39] and decreasing pain medication usage.[38,39] The strength of a SNS response from DN is directly proportionate to the strength of the stimulation.[36] DN should provide a more substantial mechanical stimulation than the placebo, and therefore all measures of SNS activity should be heightened. This translates to a decrease in HRV, an increase in EDA, and increase in PPT, and a decrease in ST. There is conflicting evidence regarding ST changes after manual therapy techniques applied to the spine, including but not limited to DN.[21,40] It appears that vasodilation, and a subsequent increase in ST, occurs in the area of referred pain, but not necessarily the entire limb.[40] A study by Skorupska et al[40] found a statistically insignificant decrease in ST of the foot after DN to the gluteus medius in subjects with active MTrPs, despite finding an increase in ST in the area of referred pain for the MTrP that was treated. The referral pattern of TL multifidi does not include the foot; therefore it is unlikely that DN to the multifidi in this dissertation study would cause vasodilation in the foot that would confound the results.

H_2: Subjects who receive DN to the TL junction will have a greater improvement in fingertip to floor (FTF) measurement, passive straight leg raise (SLR) and passive knee extension (KE) measurements from baseline than subjects who receive sham DN.

Intrafusal fibers within muscle spindles respond to changes in muscle length, and have been shown to have autonomic innervation, in addition to sensory and motor innervation.[41,42] Studies looking at electrical or physiological activation of the SNS show mixed results on how the SNS impacts muscle spindle sensitivity.[43-49] Some studies indicate a decrease in muscle

spindle sensitivity with SNS activation, however these studies have used anesthetized rats, rabbits, or cats.[42-45] Studies on humans have shown no change or an increase in muscle spindle sensitivity, however the sample sizes have been very small.[46-49] In studies on humans, none have investigated physiological activation of the SNS in the area where the primary SNS supply of the tested limb is located.

H_3: DN to the TL junction will create a greater sympatho-excitatory effect in the LE when compared with the UE, as measured by PPT.

A SNS discharge at a spinal segment is theorized to have the greatest impact on structures that are connected to that segment.[25] This has been supported by Srbely et al[50] when they found statistically significant improvements in PPT of the supraspinatus immediately following DN to the infraspinatus (both innervated by C5), but no statistically significant changes in gluteus medius PPT (innervated by L4-S1) ipsilaterally when compared with sham DN. Bialosky et al[51] found similar results in their study, during which they compared how lumbar spinal manipulation affects thermal pain sensitivity segmentally and extra-segmentally. Subjects in the spinal manipulation group experienced a significant increase in hypoalgesia in the LE when compared with subjects who rode a stationary bike or were given extension exercises, however there were no significant between-group differences in hypoalgesia in the UE.[51] The sympathetic nerves that impact the UEs originate from T2-T6, but possibly as inferior as T8, and thus the UE should not be affected by treatment to the TL junction.[31] With SNS stimulation comes the release of catecholamines into the blood stream by the adrenal medullae.[31] This may result in some change in extra-segmental pain modulation to the UE after lumbar manipulation, however it is unlikely to be equivalent to the LE because of its lack of segmental relationship to the lumbar spine.

H_4: There is a relationship between immediate changes in sympathetic outflow, as measured by low frequency to high frequency (LF:HF) ratio of HRV immediately post-treatment, and GRC, ODI, and pain rating at 24-hour follow-up.

If changes in sympathetic outflow are part of the mechanism responsible for the clinical improvements that patients experience after DN, then there should be a relationship between sympathetic outflow and improvements in clinical outcomes questionnaires. Also, the changes that occur after any treatment should be meaningful to patients, and outcomes questionnaires are an excellent way to quantify this. Three common questionnaires used in research and clinical practice are the GRC, the ODI and the Numeric Pain Rating Scale (NPRS). GRC has good face validity and highly correlates with a patient's measurement of how important the change is to him or her.[52] GRC is a subjective measure of overall improvement and correlates with objective measures, such as the ODI (r=0.78),[53] and physical performance tests, such as the hop test (r=0.58).[54] LF:HF ratio indicates the ratio of output from the two branches of the ANS, and is a good indicator of which branch of the ANS is dominant.[55,56]

DEFINITION OF TERMS

- Dry needling – a direct method of MTrP treatment using a filament to penetrate muscle tissue greater than 1 cm, which often elicits a LTR within the muscle being treated.[57]
- Low back pain – primary area of pain at or below T12 to the sacrum.
- Needle effect – the immediate analgesic effect of treatment with a needle is independent of the substance being injected, or if a substance is being injected.[2]
- Myofascial trigger point – "a hyperirritable spot in a skeletal muscle that is associated with a hypersensitive palpable nodule in a taut band. The spot is tender when pressed and

can give rise to characteristic referred pain, motor dysfunction, and autonomic phenomena."[58]

- Needle manipulation – movement of the needle after it has penetrated the target tissue, including but not limited to pistoning, rotation, and pecking.
- Local twitch response – a contraction in a taut band of muscle that is mediated by the central nervous system, which can be elicited by palpation or DN.[7,8]
- Pistoning – another name for the needle manipulation popularized by Hong.[9] It involves manipulating the needle up and down rapidly at a speed of 1-2 times per second, without fully withdrawing the needle from the skin.[59]
- Decreased hamstring length – a deficit in hamstring length of greater than or equal to 15 degrees, as measured by KE.

EXPLANATION OF VARIABLES

Independent Variables

- Dry needling – insertion of a thin filament into the multifidus followed by 15 seconds of pistoning, to be performed at the T12 and L1 segments bilaterally.
- Sham dry needling – the use of a non-penetrating "needle" to simulate the stimulation that occurs with dry needling at the T12 and L1 segments bilaterally.

Dependent Variables

- Heart rate variability – an indicator of autonomic regulation of heart rate.[55,60] This includes time domain measures of root mean square of the successive differences (rMSSD) and standard deviation of peak to peak (SDPP), as well as the frequency domain measure of LF:HF ratio in this dissertation study.

- Pressure pain threshold – the minimum force applied to one's body which induces pain, as measured by an algometer.[61]
- Skin temperature – a measure of cutaneous circulation, which is mediated by the sympathetic vasoconstrictor and vasodilator nerves, which is measured using a skin thermistor.
- Electrodermal activity – measurement of the electrical potential of the skin by quantifying the time for an impulse to pass between two points.[62]
- Fingertip to floor – a measure of simultaneous lumbar and pelvic mobility, measured by the distance from a subject's most distal finger to or past the top of a raised platform.[63]
- Straight leg raise – the most common clinical test used for hamstring length,[64] in which the leg is flexed at the hip, with the knee fully extended and ankle resting in plantarflexion.[65]
- Knee extension – a measure of hamstring flexibility, in which the thigh is positioned perpendicular to the treatment table and the lower leg is passively extended until resistance is felt.[65]
- R_1 – the first point of resistance that is felt when a muscle is being lengthened.
- R_2 – the point of maximum pain-free range of motion when a muscle is being lengthened.
- Modified Oswestry Disability Index – a 10-item questionnaire used to quantify one's functional disability from LBP, which is commonly used in research and in the clinic.[53,66]
- Global Rating of Change – a scale used in research and in the clinic to quantify a summation of a patient's improvements in pain, disability, and quality of life.[52]

- Numeric Pain Rating Scale – an 11-point scale commonly used to quantify pain levels in patients with musculoskeletal conditions, with anchors of "no pain" and "worst pain imaginable."[67]

Covariates

- Needle anxiety- a feeling of fear associated with skin puncture, which is often associated with changes in heart rate, blood pressure and stress hormone secretion. This is not the same as needle phobia, which includes an avoidance of medical care resulting from the anxiety of skin puncture.[68,69]

STUDY RATIONALE

This is a timely study given that more focus is being placed on the SNS effects of manual therapy, and how it affects body regions distant to the site of treatment. DN is becoming more common in PT practice, and a better understanding of the mechanisms of action would help clinicians to understand to whom and under what circumstances a treatment will be most effective. Additionally, studies of DN have used small sample sizes, making the studies under-powered, or have included healthy subjects, which do not represent the typical clinical population. This dissertation study included an adequate sample size and a sample from a clinical population.

SUMMARY

As DN becomes a more common treatment method for musculoskeletal dysfunction from MTrPs, more research needs to be done to understand the pathways on which it works. Much of the available research on how manual therapy affects the SNS has focused on joint mobilization or manipulation and its effect on indicators of SNS activity in the UE,[5,13-15,17,18] and in the LE to a lesser degree.[16,19,20] Available studies on SNS stimulation and how it affects intrafusal muscle

fibers uses samples of rats, rabbits and cats in various states of consciousness.[42-45] Other studies that have used samples of human subjects that may have been too small to achieve adequate statistical power.[20,46-49] There is a need for high-quality studies that investigate the neurophysiological effects of DN to the TL junction in human subjects.

This dissertation study would add to the understanding the therapeutic effects of DN of the TL junction paraspinals on the LEs. The TL junction is the origin of the SNS output for the LEs.[31] Currently there is very limited research on how treatment to the TL junction affects the LEs.[70] The potential for alternative methods of pain control is paramount given the opioid crisis the United States that is facing at this time. There is evidence that the hypoalgesic effects of DN are segmentally-related,[50] and DN to the TL junction could provide a powerful response in areas that are segmentally-related via autonomic innervation.

CHAPTER 2: REVIEW OF THE LITERATURE

INTRODUCTION

Manual therapy is a treatment modality used by physical therapists (PTs) to impact the musculoskeletal and nervous systems. One branch of the nervous system that can be affected by manual therapy is the autonomic nervous system (ANS). The ANS is the involuntary nervous system and is divided into two branches: the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS). Both systems can influence most tissues in the human body, however the SNS is capable of a more profound effect because it has longer postganglionic neurons, it has a high postganglionic to preganglionic neuron ratio, and it causes the adrenal medulla to release epinephrine and norepinephrine directly into the blood stream, which can then travel to all body systems.[71] This chapter presents the review of the literature relating to how manual therapy affects the SNS, and it involves discussion of different forms of manual therapy because of the limited number of studies on how dry needling (DN) affects the SNS.

NEUROPHYSIOLOGICAL EFFECTS OF MANUAL THERAPIES

Until recently, researchers were more interested in the local effects of manual therapy, such as tissue lubrication and relaxation, or correction of a segmental subluxation.[18] There has been a paradigm shift in manual therapy rationale toward considering the effects of manual therapy on multiple body systems, including the nervous system. The neurophysiological effects of manual therapy can be peripheral, spinal, or supraspinal (**Figure 1**).[72] Peripherally, manual therapy can change serum levels of endogenous cannabinoids, serotonin, substance P and other mediators of pain and inflammation. Manual therapy can act on the spinal level as a counterirritant; the input from proprioceptors during manual therapy can bombard the spinal cord with additional sensory input. Supraspinal structures involved in pain processing, such as the

amygdala, periaqueductal gray matter, and the anterior cingulate cortex, are less responsive after manual therapy.[72]

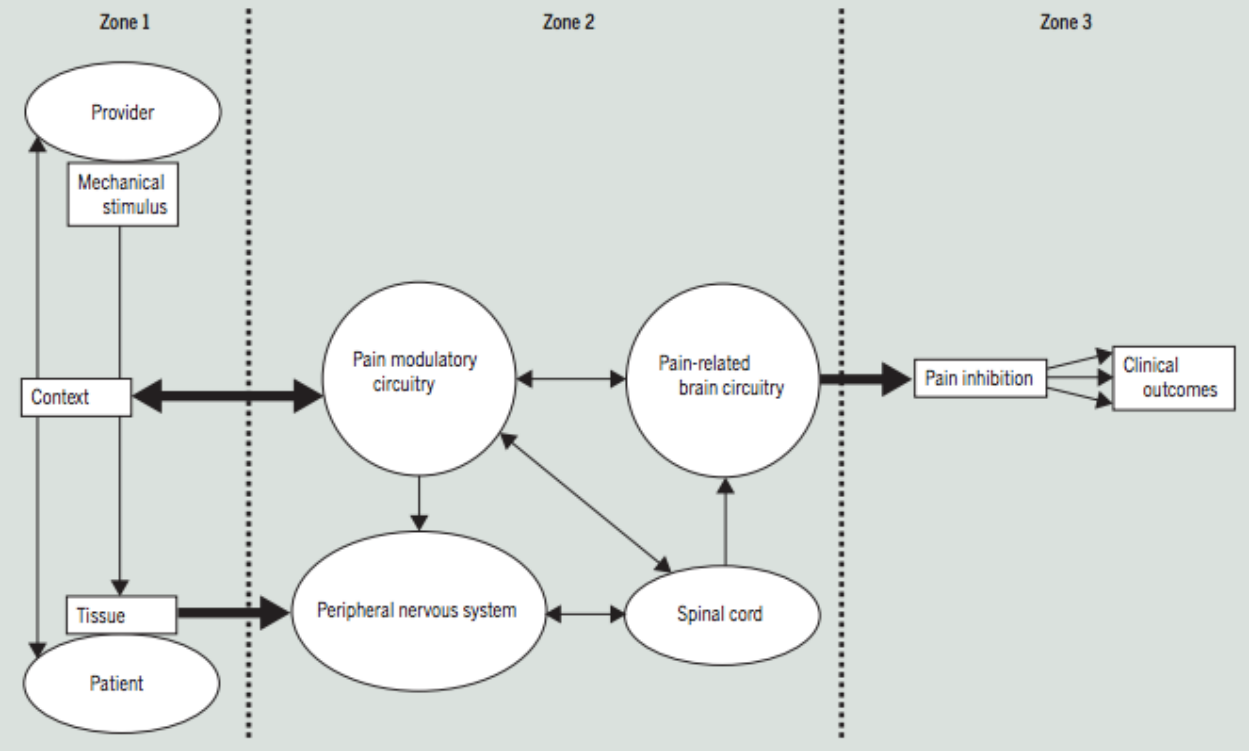

Figure 1. A model of the mechanisms of manual therapy. Mechanical stimulation of tissue can create a cascade of neurophysiological effects.[72]

Spinal Mobilization and Manipulation

Sympatho-excitation from joint mobilization leads to changes in physiologic measures in multiple body systems. In an asymptomatic population, this can present as decreased mechanical nociception, increased electrodermal activity (EDA), increased respiration rate, increased heart rate (HR), decreased skin temperature (ST), increased muscle blood flow, and analgesia via descending non-opioid pathways.[11-14,17,20] One must use caution when generalizing these findings to a symptomatic population, as many of the studies have not included subjects with pain.[12-16] A

frequent topic in the currently available research on the neurophysiological effects of manual therapy has been joint mobilization to the cervical spine, specifically C5.[12,14,15,17,73] The results of these studies should not be generalized to treatment other areas of the spine, including the TL junction. This dissertation study was designed to investigate neurophysiological effect manual therapy directed to the primary location of SNS outflow to the lower extremity (LE), and its potential value in treating patients with LE musculoskeletal conditions.

Research has shown that oscillatory mobilizations at a higher rate yield a greater SNS response than sustained mobilizations or oscillations at a lower rate.[11,15,16] Higher SNS response is more likely to be associated with a greater activation of descending pain controlling mechanisms.[74] Because oscillatory joint mobilizations created a greater SNS response than sustained mobilizations,[11] a dynamic DN technique was chosen for this dissertation study.

Comparatively, there is more research on the neurophysiological effects of spinal manipulation when compared with DN. Bialosky et al[75] found no significant change in mechanical pain sensitivity tested via pressure pain threshold (PPT) locally and remotely, but did find a change in thermal pain sensitivity in subjects who underwent spinal manipulative therapy when compared with placebo. A systematic review and meta-analysis by Coronado et al[76] suggested that there is a greater remote response to mechanical pain sensitivity after spinal manipulation when compared with local response in both symptomatic and asymptomatic subjects. Their study adds to the body of research supporting a change in nociceptive afferent processing within the central nervous system. However, it is worth noting that 85% of the studies used in their systematic review and meta-analysis analyzed changes immediately after manipulation, and therefore these results may not be relevant to a clinically meaningful outcome over time.

Dry Needling

In comparison to the studies on the neurophysiological effects of spinal mobilization and manipulation, there have been relatively few studies on the neurophysiological effects of DN.[22-24] Like spinal mobilization, DN affects the sensory, motor and autonomic nervous systems, and the effects may be local, segmental, and extra-segmental.[6,22,23,36,77] A visual representation of these effects can be seen in **Figure 2**. Local effects may include an increase in local blood flow[10] and a decrease in spontaneous electrical activity at dysfunctional motor endplates, which could lead to relaxation of the muscle being treated.[10,78,79] DN is believed to stimulate A-nerve fibers for up to 72 hours after treatment, and the prolonged stimulation causes an opioid-mediated inhibition of pain via dorsal horn interneurons. DN blocks afferent noxious stimulation to the dorsal horn via activation of noradrenergic and serotonergic descending inhibitory pathways.[6]

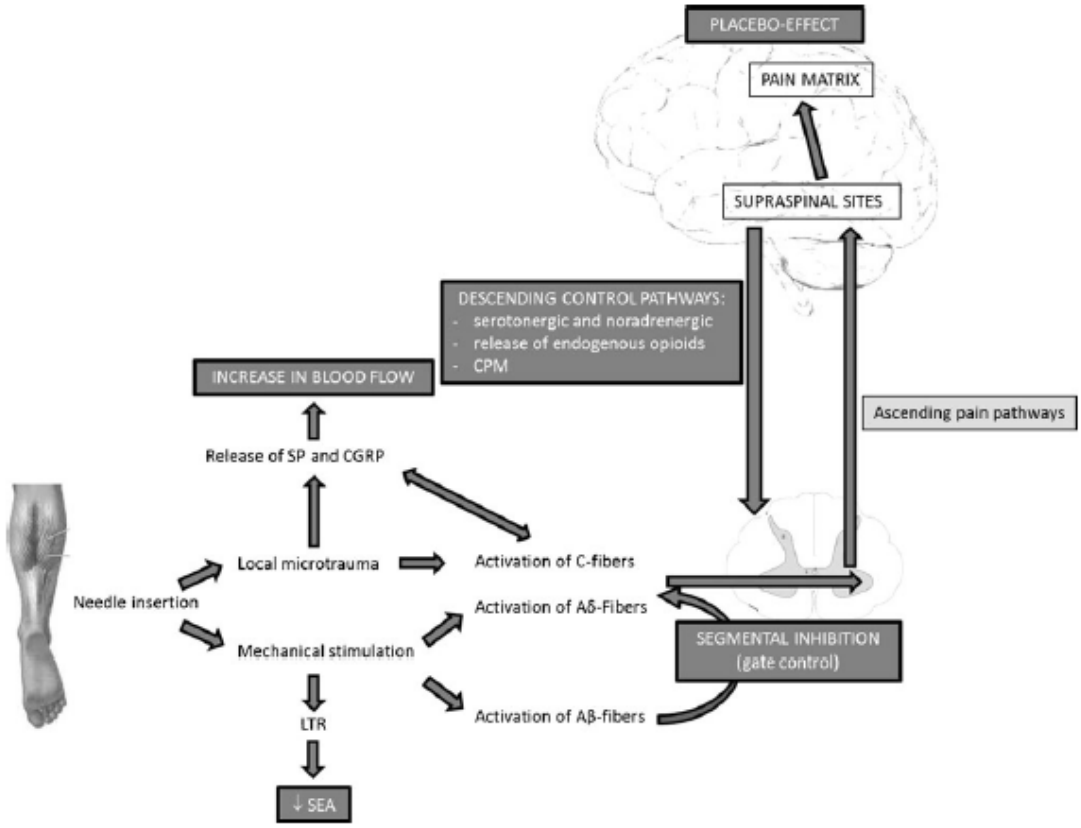

Figure 2. Potential neurophysiological effects of DN.[10]

The data on the neurophysiological response to DN are mixed. Some studies have looked at the ANS effect of DN and found a down-regulation of SNS activity. Both studies included subjects who have had myofascial pain in the upper trapezius for 3 to 6 months or longer.[22,23] It is possible that the presence of active MTrPs for this duration up-regulates the SNS, and this could explain the decrease in SNS activity after DN. Another study investigating changes in PPT had shown no significant difference between DN and ischemic compression, which is a non-invasive technique commonly used in the treatment of MTrPs.[24] Small sample size, lack of standardization of the rate of pressure, and examining only local effects of treatment should be considered when generalizing the results.[22,24] Another study included only subjects who have had a stroke, and they found a statistically significant improvement in widespread pressure pain threshold after a single session of DN, which supports a central antinociceptive effect.[77] Future studies, such as this dissertation study, should be performed to further understand the remote antinociceptive effects of DN concurrent with sympatho-excitation.

MEASURES OF AUTONOMIC NERVOUS SYSTEM ACTIVITY

Heart Rate Variability

HR is controlled by the ANS, with both the SNS and PNS contributing to elevate or decrease the HR, respectively. Under normal circumstances at rest, the PNS dominates and the heart rate is slowed. The human cardiovascular system is capable of rapid adjustment in times of stress or relaxation.[80] Heart rate variability (HRV) is defined as the variation in time between heartbeats. In other words, HRV is the time difference between two consecutive heartbeats, when compared with the mean time between heartbeats determined by HR.[81] HRV at rest is high in the absence of physical or emotional stress because the SNS impulses to cardiac tissue are too slow

to produce beat-to-beat changes.[82] High HRV is also a symptom of some medical conditions such as atrial fibrillation,[80] however subjects with this diagnosis were excluded from this dissertation study to avoid confounding the results. Researchers have proposed HRV to be a reliable and valid measure of adaptive regulation of the ANS.[83]

Both time domain and frequency domain measures should be considered when analyzing HRV statistics.[81] Time domain measures are simple to compute but lack the ability to differentiate which part of the ANS is predominately driving the HRV.[81] Frequency domain measures are broken down into four categories, however this dissertation study only investigated high frequency (HF) and low frequency (LF) bands. HF bands show the contribution from the vagus nerve, relating to the PNS, and LF shows the contribution from SNS.[81] The ratio of low to high frequency (LF:HF) is said to reflect the balance between the two systems of the ANS. There is a very-low frequency domain, however because it receives contributions from chemoreceptors and the renin-angiotensin system as well as the SNS[55,81] it was not included as part of the analysis in this dissertation study.

Skin Temperature

Skin temperature (ST) is a simple and non-invasive way to detect peripheral vasoconstriction from an increase in sympathetic outflow. Sympathetic fibers primarily innervate the vascular smooth muscle of the blood vessels. During SNS activation, the smooth muscle constricts and blood flow is diverted away from the skin to prevent blood loss in trauma and to make blood more available to internal organs and working muscle; this would present as a decrease in ST.[84] Additionally, DN is believed to activate the periaqueductal gray in the midbrain, which is responsible for thermoregulation.[10] ST has been used previously as an outcome measure in the SNS effect of manual therapy.[15,17,85-87] A systematic review of 11 studies

on this topic showed a moderate to large effect size for manual therapy directed to the cervical and thoracic spine.[88]

Pressure Pain Threshold

PPT is one method of quantitative sensory testing, which detects changes in pain processing and modulation. It is one of the more common outcome variables used in studies on how SNS activation induces hypoalgesia after manual therapy, and is widely used in a clinical setting.[89] PPT algometry has been found to have excellent intrarater reliability in patients with knee pain (ICC=.93-.97),[90] healthy subjects (ICC=.94-.97),[91] and patients with neck pain (ICC=.96-.97),[91] however PPT can vary by factors, including but not limited to biological sex, age, pain intensity and dominant versus non-dominant limb.[91] Research shows that inter-rater (ICC=.79-.90) and test-retest reliability (ICC=.76-.79) are also adequate after as little as 1 hour of training.[91]

The literature indicates that pain modulation after DN can occur locally,[22] segmentally[50,92,93] and extra-segmentally.[29,77] The studies showing segmental effects tested remote locations that were either myotomally or dermatomally related to the treated muscle. To date, no study has looked at the segmental effects of the SNS on remote PPT.

Electrodermal Activity

EDA is the quantity of electrical activity that can be detected on one's skin in response to changes in secretion of sweat.[94] It can be measured at rest, but increases when the SNS is stimulated and the sweat glands become more active.[95] Sweat glands are located throughout the body and are purely innervated by the SNS, which explains why EDA is a widely used dependent variable in physiological studies of SNS arousal.[96] The eccrine sweat glands are most concentrated in the palms of the hands and the soles of the feet.[96] Sweat glands secrete primarily,

but not exclusively, salt water, which increases the electrical conductivity of the largest organ in the human body. It is a sensitive, non-invasive and easy method to measure sympathetic arousal,[95] and it is arguably one of the best measures of sympathetic arousal because it does not receive input from the PNS.[62,97] EDA has been used previously in studies examining the neurophysiological effects of manual therapies.[13,15-17,20,22,86,98]

SYMPATHETIC NERVOUS SYSTEM EFFECT ON SKELETAL MUSCLE

Over a century ago, scientists started to hypothesize the existence of sympathetic innervation of skeletal muscle and its influence on motor control.[99] Only recently has it been proven that intrafusal muscle fibers in human lumbricals, biceps, levator scapulae, and deep neck muscles have direct sympathetic innervation.[41] In mammals, there exists separate fusimotor innervation for muscle spindles, in addition to the skeletomotor innervation. The benefit of this separate innervation is that more detailed information about movement can be processed independently.[46]

The literature yields conflicting results on how the SNS affects skeletal muscle, specifically the muscle spindle afferents.[42,100] Much of this research has been performed in decerebrate or anesthetized rabbits, rats and cats. The results should be extrapolated with caution because they may not represent the effects on conscious humans in various states of attention and emotion.[42-45,47,101]

In non-human vertebrates, sympathetic nerve stimulation decreases the mean discharge rate of muscle spindle afferents in 70-85% of motor units, and the remaining motor units had no change in discharge rate.[42,44] The mean discharge rate remained depressed until up to 4 minutes after stimulation to the sympathetic nerve ended.[44,45] Nearly half of the motor units became electrically silent for up to 160 seconds.[44] Injection of succinylcholine normally creates a

transient increase in muscle spindle afferent discharge, however the data show SNS stimulation was able to override this and still create a depressant effect.[45] This may be beneficial and desirable in a fight or flight response; limiting one's ability to control muscle length changes sacrifices fine motor control to allow for greater power or speed.[41,45]

The changes in muscle spindle afferent discharge rates appear to be independent of blood flow changes within the muscle.[42,45] Because blood vessels in the skeletal muscle do not have α receptors for vasoconstriction, they do not constrict with SNS stimulation. The lack of vasoconstriction allows increased oxygen and nutrition to working skeletal muscles during a flight or flight response.[71] Blood flow can be occluded ipsilaterally and bilaterally while monitoring muscle spindle afferent discharge, and there was no change in resting discharge in nearly all the motor units.[45]

Studies that do not support a change in fusimotor tone in humans have used methods of SNS stimulation like mental computation or the Valsalva maneuver, which may not provide enough SNS stimulation to make a statistically significant change.[46,48] Of the studies on humans, some have used sample sizes of only 8-10 subjects, and there may not have sufficient statistical power.[48,101] The direct sympathetic nerve stimulation performed by Roatta et al[45] mimicked physiological activation rates, and therefore this data may be more appropriate to generalize to physiological activations of the SNS. To date, no study has investigated the SNS effect of DN directed to the primary location of outflow for the LE.

DRY NEEDLING THEORETICAL FRAMEWORK

The spinal cord is connected to the SNS via 14 spinal nerve roots from T1-L2, therefore the outflow of the SNS is heavily influenced by dysfunction at or treatment to the thoracic and upper lumbar spine.[31] In his radiculopathy model of DN, Dr. C. Chan Gunn states that the most

critical muscle shortening occurs at the paraspinal muscles.[25,102] In his theoretical model, he states that shortening of these muscles compresses the intervertebral disc and the nerve root (**Figure 3**). This could start a cyclic phenomenon because nerve compression leads to radiculopathy, which leads to shortening of the paraspinal muscles, which in turn leads to more compression of the disc and nerve root.[25] Because nerve compression leads to a decrease in transmission of nerve impulses, the compression may affect the motor, sensory, and autonomic nerves associated with that segment.[25] Innervated structures would no longer receive the impulses they need to maintain proper cellular function. This can result in "disuse supersensitivity" of the structures that are affected by that nerve.[25] Ganglia of the SNS would be no exception to disuse supersensitivity. A potential consequence of supersensitivity of the SNS ganglia is overstimulation of the adrenal glands, cardiac muscle, sweat glands and skeletal muscle.[25] For skeletal muscles, this can manifest in spontaneous electrical activity, which maintains the muscle in a perpetual state of partial contraction.[102]

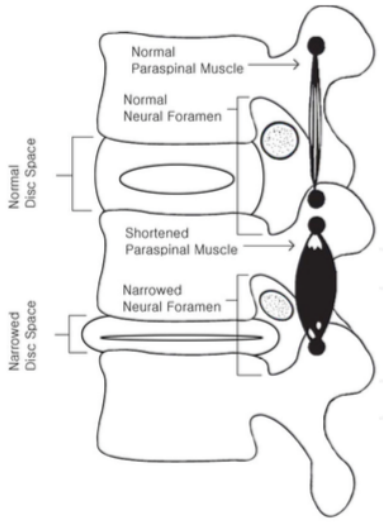

Figure 3. As stated in Dr. C. Chan Gunn's radiculopathy model of dry needling, a shortened paraspinal muscle compresses the nerve root by narrowing the disc space and the neural foramen.[103]

REGIONAL INTERDEPENDENCE

Development of the biomedical model has been beneficial for treatment and eradication of many diseases, however it has not had the same effect on musculoskeletal disorders.[104] PT researchers have proposed a model of "regional interdependence."[104-106] Regional interdependence is the concept that "a patient's primary musculoskeletal symptom(s) may be directly or indirectly related to or influenced by impairments from various body regions and systems, regardless of the proximity to the primary symptom(s)."[106] Regional interdependence also implies that the musculoskeletal system can be affected by the peripheral and central nervous systems, and that changes in the musculoskeletal system accompany changes in the neurophysiological system.[105,106] There is evidence that treatment to proximal body structures can be used to treat distal pain because of a connection between increased SNS activity and pain modulation.[11]

Research suggests that there is a complicated relationship between the biomechanical and neurophysiological effects that can occur with regional interdependence.[107] Musculoskeletal system function can be affected not only by other musculoskeletal structures and neurophysiological structures, but also biopsychosocial and somatovisceral systems (**Figure 4**).[106] The revised model of regional interdependence shows psychosocial factors and patient expectations can influence the musculoskeletal response to treatment, however those factors will not be discussed because they are beyond the scope of this study.

Although isolated thoracic spine dysfunction does not account for a large percentage healthcare dollars spent, it is often thought that the thoracic spine is a "silent contributor" to other musculoskeletal conditions.[32] There is a growing body of evidence supporting that treatments applied to one anatomical region can influence seemingly unrelated areas, and much

of the research relating to the LE has investigated contributions from the lumbopelvic region.[106] To date, a single case study describes and theorizes a link between LE musculoskeletal symptoms and SNS stimulation resulting from dysfunction in the lower thoracic spine.[70] Ignoring the potential contribution of dysfunction in the thoracic spine to injury could be a reason there is so much variability in patient outcomes for treatment of extremity disorders.[104] More research needs to be performed on the contribution of the thoracic spine to dysfunction in the lower quarter.[32]

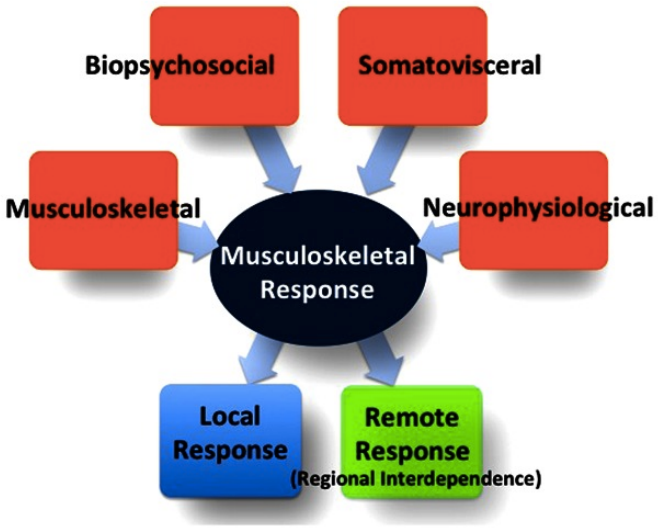

Figure 4. The revised model of Regional Interdependence, which emphasizes a remote response.[106]

SAFETY OF DRY NEELDING

In terms of adverse events (AEs), DN has been compared to acupuncture. There has been more research on AEs from acupuncture than with DN, but the types of AEs are similar. Acupuncture differs in technique, depth and location of treatment, and underlying treatment philosophy. Therefore, the results of acupuncture studies cannot always be applied to DN.[108] The most common serious AEs are pneumothorax, spinal cord lesions, and peripheral nerve or blood

vessel injuries, however many of these can be avoid if clinicians have proper knowledge of anatomy and apply their knowledge appropriately.[109] As with any invasive treatment, with DN there is a possibility of infection. There is no evidence to suggest significant infections occur through DN since hand washing, personal protective equipment, single-use sterilized needles and proper disposal procedures have become the norm.[2,110] Cases of serious bacterial infection have been reported, but they are rare and often the result of negligence or a provider's lack of training.[2,109,110] In the United Kingdom, there have been no reported cases of human immunodeficiency virus, Creutzfeldt-Jacob Disease or hepatitis C virus resulting from acupuncture treatment.[110]

In a study by Brady et al,[108] out of 7,629 DN treatments, of which 82.7% were DN, there were 1,463 AEs (19%). In this study an AE was operationally defined as "any ill effect, no matter how small, that is unintended and non-therapeutic."[108] The most common AEs reported were bleeding, bruising, and pain during or after treatment.[108] All AEs were minor and did not cause any alteration in function, however the frequency derived from this study can be described as "very common." Lower rates have been reported in other studies, and the difference in rates may be attributed to having PTs or patients report the occurrence of an AE. Patients are less likely to report an event that doesn't result in a change in function.[108]

A significant AE is one that lasts longer than 2 weeks and requires additional medical treatment. Because there were no significant AEs in the study by Brady et al, a calculation was used to determine the risk of a significant AE. The estimated risk of a significant AE based on the study's sample is less than 0.04%.[108] Another study specifically addressing AEs in DN by physicians and PTs found minor AEs occurred less often (6.7%) than Brady et al's study, and found a slightly higher rate for more serious adverse events (0.14%).[111]

The most common mild AEs are bleeding more than a drop (3%), symptom irritation (1-2%), needling pain of more than a little sharpness (1%), drowsiness (<1%), and faintness (<0.5%).[36] When needles are used in an area of edema, cellulitis can occur. This is uncommon,[36] and subjects with visible edema in the area to be treated were excluded to eliminate this risk factor. While there are risks associated with DN, it should be considered as an alternative pain-relieving treatment to NSAIDs, which carry a four-fold increase of gastrointestinal bleeding, as well as increased risks of hypertension and stroke.[36] The risk of AEs caused by aspirin and other analgesics is substantially higher as well.[108]

Iatrogenic pneumothorax is a rare but serious potential side effect of DN, and the risk can be reduced with proper palpation and with adequate training of those administering the technique.[112] The World Health Organization regards the risk of pneumothorax from DN or acupuncture to be "very rare," with an incidence of less than 1 in 10,000. Large prospective studies have shown rates of pneumothoraces to range from 1 in 69,994 to 1 in 1,170,000.[112] A pneumothorax occurs more frequently with needling to the supraclavicular and infraclavicular regions, and the parasternal region.[109] This dissertation study did not involve treatment to any of those areas. All risks were disclosed to each subject before informed consent was obtained. Any concerns were discussed and subjects had the ability to withdraw from the study at any time.

SUMMARY

Manual therapy techniques, including but not limited to DN, can have profound influences on the nervous system, and their therapeutic effects should not be discounted. The mechanisms that govern pain modulation after manual therapy, including DN, are not fully understood. Researchers have proposed that activation of the SNS with manual therapy can result in pain modulation and flexibility changes, however available studies have their methodological

flaws. There have been relatively few studies on the sympathetic effects of DN when compared with the available literature on the sympathetic effects of mobilization and manipulation. Changes in SNS activity after manual therapy can be monitored indirectly by non-invasive monitors for EDA, ST, HRV and PPT.

Recent treatment models, specifically the model of regional interdependence, have considered the neurophysiological effects of the PT interventions. Regional interdependence refers to the idea that many areas, both near to and far from a patient's primary complaint of pain, can be contributing to his or her symptoms.[104,106] The effect of treatment to the thoracic spine on neck and shoulder pain has been researched,[105] but more studies are necessary to determine if treatment to the TL junction is beneficial for LE dysfunction.

Any invasive treatment carries a risk of an AE. The risk of a minor AE from DN is low, and a significant AE is very rare.[108,111] Risk of infection or iatrogenic pneumothorax is very low.[110,112] Much of the risk of an AE can be mitigated with adequate knowledge of anatomy and consistent application of anatomical knowledge to clinical practice.[109] This dissertation study did not involve treatment to parasternal, supraclavicular or infraclavicular regions, which are most often associated with iatrogenic pneumothorax.[109]

CHAPTER 3: METHODOLOGY

INTRODUCTION

This chapter introduces the methodology used for this dissertation study. The methodology, including aspects of the design, independent and dependent variables, as well as how they were measured, were carefully selected to maximize reliability, validity, and feasibility.

STUDY DESIGN

This dissertation study was a prospective, double-blind randomized clinical trial.

FUNDING

This dissertation study received no external funding.

STUDY SETTING

This dissertation study was conducted at Sports and Orthopaedic Therapy Services, LLC in Kensington, Maryland. This was the location of employment of the primary investigator. Data collection was performed in a temperature-controlled private treatment room within the clinic during non-operational hours to minimize noise and interruptions for the investigator and the subjects. This also allowed for confidentiality of study participants. All data collection occurred on a consecutive Saturday and Sunday.

SUBJECTS

Eligible participants were individuals, ages 18 to 70 years inclusive, with low back pain (LBP) and decreased hamstring length, which was operationally defined as at least one hamstring having greater than 15^{o} restriction at R_1. LBP was operationally defined as pain at or below T12. Individuals with pain at the sacroiliac joint in the absence of LBP were not eligible. Subjects

were accepted consecutively, and data collection continued until the desired number of subjects had been reached.

Power and Sample Size

A power analysis was completed using G*Power (Version 3.1.9.3). Sample size calculation was based on the primary outcome of sympathetic nervous system (SNS) activity. Pressure pain threshold (PPT) was chosen as the primary endpoint because there is the most available data pertaining to PPT after dry needling (DN) treatment. Based on the findings for ipsilateral changes in PPT by Salom-Moreno et al[77] when compared with a control group, 27 subjects in each group (total 54 subjects) were required to detect a large effect size (d=0.8) in PPT between the 2 groups with an alpha level of .05 at a power of 0.8.

Inclusion and Exclusion Criteria

As stated previously, the inclusion criteria for eligibility for this dissertation study were having LBP, having decreased flexibility greater than or equal to 15^{o} at R_1 in at least one hamstring, as measured by passive knee extension (KE), and being between the ages of 18 and 70 years inclusive at the time of participation. The upper limit for age was based on changes that occur with aging, including a decrease in function of neurotransmitters and a decreasing number of neurons and axon branches throughout the body.[113] Elderly adults also experience a rapid decline in upper extremity (UE) and lower extremity (LE) flexibility starting in the 8^{th} decade of life, specifically with substantial yearly declines in the LE starting at age 71.[114]

Exclusion criteria were local skin lesion or edema, local or systemic infection, previous treatment of DN to any body part, history of abnormal bleeding, presence of radicular symptoms, prescription anticoagulant therapy, autoimmune disease, pregnancy, previous surgery to lumbar spine, inability to read and understand English, and cognitive impairment that would limit the

ability to give consent.[115] Subjects with multiple sclerosis and other central nervous system lesions were excluded because of the likelihood that sympathetic pathways were affected.[23] Subjects with diabetes mellitus were excluded because measurements of autonomic nervous system (ANS) activity have been shown to have high variability from right to left extremities in this population.[116] Subjects were also excluded if they had a body mass index of greater than 30 kg/m^2 because excessive subcutaneous fat decreases palpatory accuracy for experienced and novice clinicians (p=.0003).[117]

Prior experience with DN may influence a subject's ability to distinguish between placebo and treatment. Sham DN should not produce a local twitch response (LTR), and if a subject had experienced LTRs before, he or she will likely identify the sham procedure. As a part of the 24-hour follow-up measurements, subjects were asked which condition they believed to have received to confirm that the placebo was indistinguishable from DN. Subjects with fear and anxiety associated with needles were allowed to participate, however because fear can increase SNS activity[22] it was quantified with a numeric rating scale prior to participation and included in the statistical analysis for outcomes relating to the SNS.

Recruiting Procedures

Subjects were recruited via advertisements placed in outpatient physical therapy clinics throughout Montgomery County, Maryland. Eligibility was confirmed with a brief questionnaire in person, over the phone, or via email. Eligible subjects that were interested in participation were emailed all required paperwork, including the informed consent document for their review.

INSTRUMENTS AND MEASUREMENTS

Sympathetic Nervous System Outcomes

Pressure Pain Threshold. PPT was measured by a Wagner FPX^{TM} digital algometer (Wagner Instruments, Greenwich, CT, USA). PPT was measured in kilograms. Measurement of PPT immediately after DN may be influenced by post-treatment soreness locally,[118] however the results of this dissertation study would not be confounded because the site of PPT testing is remote from the treatment location. The minimum detectable change (MDC) in PPT in the LE, specifically the tibialis anterior, is 1.00 kg/cm^2.[91] It should also be noted that repeated algometer testing of PPT does not have a significant effect on SNS regulation of pain perception.[119]

Electrodermal Activity. Electrodermal activity (EDA) is the best measure of sympathetic arousal because the sweat glands have only sympathetic innervation, therefore there is no contribution from the parasympathetic nervous system (PNS). The tonic level of EDA was used in this dissertation study because it is an indicator of general autonomic arousal and is appropriate for subjects at rest in the absence of stimuli.[62] The electrodes used were Ag-AgCl electrodes with isotonic gel. They were placed on the plantar surface of the foot on LE that had the greatest hamstring restriction.[120] All data collection was performed at the same time on Saturday and Sunday to avoid cofounding the data by the daily rhythms of EDA.[96] Sampling rate was set to 1,000 Hz.

Heart Rate Variability. Heart rate variability (HRV) refers to changes in heart rate and interbeat intervals,[55] and was used in this study as a method of quantifying SNS activation. HRV was measured by measuring peak-to-peak intervals of a pulse waveform using photoplethysmography (PPG). For the purpose of analysis, 5-minute time intervals were

established in this dissertation study because it is the duration accepted for short-term recordings according to the Task Force of the European Society of Cardiology.[55,80]

The standard deviation of peak-to-peak intervals (SDPP) and the root mean square of the successive differences (rMSSD) during the baseline phase and post-treatment phases on Day 1, and a follow-up phase on Day 2, were recorded. Subjects were monitored during the treatment phase, but it was not part of the analysis for this dissertation study. SDPP and rMSSD are among the most commonly used time-domain measurements in HRV.[55,56] Frequency domain measurements, including high frequency (HF) and low frequency (LF) total spectral power, were also collected during each 5-minute recording. LF refers to spectral components between 0.04 and 0.15 Hz and is an indicator of SNS dominance.[55,56] HF refers spectral components of 0.15 to 0.4 Hz and is an indicator of PNS dominance.[55,56] The LF to HF (LF:HF) ratio was used in the analysis because it is a measure of the balance between the two branches of the ANS.[55] All of the time domain and frequency domain measurements that have been chosen were appropriate for short-term cardiovascular monitoring.[56] A systematic review of reliability for both time and frequency domain measurements has found HRV to be reliable, except in patients with chronic heart failure.[121] Sampling rate was set to 1,000 Hz.

Skin Temperature. A skin temperature (ST) thermistor transducer was taped to the dorsal aspect of the foot of the LE that has the greatest hamstring restriction, which was determined in the baseline testing. Skin thermistor measurements show excellent test-retest reliability, with the typical error being less than 0.1^{o}C.[122] Peripheral areas have a more profound change in cutaneous circulation with SNS activation,[84,123] and therefore the skin thermistor was placed distally during data collection for this dissertation study. The absence of a "gold standard"

for measuring skin temperature makes it difficult to validate specific devices.[122] Sampling rate was set to 1,000 Hz.

Flexibility Outcomes

Local Flexibility. The fingertip to floor (FTF) test was used to assess gross lumbopelvic mobility and will be performed in the same manner as Perret et al[63] in their validity and reliability study. Subjects stood with feet together on a 20-centimeter platform and were instructed to bend forward as far as they could. The distance between the most distal fingertip and the top of the platform was measured with a tape measure. In this dissertation study, a negative value denoted the subject was unable to reach the platform; a positive value denoted the subject was able to reach beyond the top of the platform. The research assistant used consistent verbal cues throughout testing. The test was repeated 3 times and the mean was recorded for analysis. The FTF test has been shown to have excellent intrarater reliability (ICC=.99).[124]

Remote Flexibility. Baseline® digital inclinometers (Fabrication Enterprises Inc., White Plains, NY, USA) were used to measure both KE and straight leg raise (SLR). KE and SLR are highly correlated (r=.63) and are frequently used in research and in the clinic to quantify hamstring flexibility.[65] All remote flexibility tests were performed 3 times at the first point of resistance (R_1) and through the full, pain-free range of motion (R_2). The mean was used for analysis. Digital inclinometry has been established in the literature as having good intrarater reliability[125,126] as well as concurrent validity when compared to goniometric measurement.[125] The MDC for digital inclinometry is 9°.[126] The MDC for SLR and KE are 6-8°.[127]

Knee Extension. KE was measured in supine similar to Mason et al[27] in their 2016 study. This method is the most reliable measurement of hamstring flexibility.[124] The subject was supine on a treatment table. A towel roll was placed under the lumbar spine to limit pelvic movement

with hip flexion. One inclinometer was placed on the midpoint of the femur, and another was placed at the midpoint between the tibial tuberosity and the distal end of the tibia. The femur was positioned perpendicular to the treatment table and fixed at 90^{o} with a 1^{o} margin of error in either direction. The lower leg was passively extended until R_1 was reached. Then the research assistant passively extended the leg to R_2.

Straight Leg Raise. For SLR, the subject remained supine on the treatment table. The inclinometer on the femur was removed. The contralateral leg remained on the table but was not anchored to the table because it has not been shown to improve the reliability of the test.[128] The towel remained positioned under the lumbar spine. The hip was flexed passively, with the knee fully extended, until the first point of resistance. The same movement was repeated for R_2.

Clinical Outcomes Measures

Outcomes measures are often used in research and in a clinical setting to determine changes after intervention.[66] Outcomes measures quantify the actual or perceived functional changes in patients, as well as their abilities to participate in work or social obligations, and manage a household.[66] Improvement should reflect not only changes in impairments like range of motion (ROM) and strength, but also their ability to perform their preferred activities. The outcomes measures used in this dissertation study were Global Rating of Change (GRC), Oswestry Disability Index (ODI), and the Numeric Pain Rating Scale (NPRS).

Global Rating of Change. GRC is a simple and convenient scale that is used in research and in the clinic to quantify a summation of a patient's improvements in pain, disability, and quality of life.[52] GRC is most frequently a 7, 11 or 15-point scale, however it has been determined that 7 to 11 points is superior in terms of patient preference, test-retest reliability, and the ability to discriminate change.[52] Anchor phrases appear on both ends of the scale, as well as a

description at the midpoint of the scale. A change of 2 points is considered the minimum clinically importance difference (MCID).[52] Preceding the scale is a question that specifically addresses the construct for the patient or subject to consider (**Figure 5**). The GRC has been shown to have excellent test-retest reliability,[129] however it has been criticized for its susceptibility to recall bias and its ability to have the patient or subject use any construct he or she chooses to determine improvement or regression.[130]

"With respect to your back pain, how would you compare yourself now to immediately prior to your dry needling treatment?"

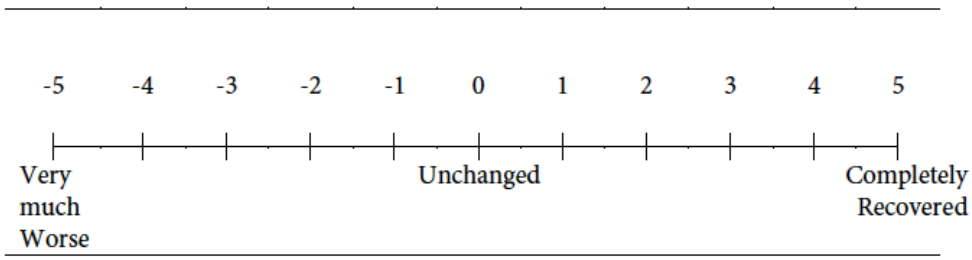

Figure 5. An 11-point GRC scale and its associated question.[52]

Oswestry Disability Index. The ODI is one of the most commonly used disability scales for patients with low back pain.[53,66] It has been found as a favorable measure for symptoms ranging from mild to severe.[131] Excellent test-retest reliability has been proven at 24-hour (r=0.99) and 4-day (r=0.91) follow-ups, and test-retest reliability decreases as the length of time before follow-up increases.[131] A modified version of the ODI will be used for this study because patients and subjects are likely to omit item 8 (sex life) in their responses as often as 50% of the time.[132] The MCID of the ODI is 6 points.[53]

Numeric Pain Rating Scale. Pain rating scales are often used in conjunction with functional questionnaires to determine patient progress in a clinical or research setting.[133] The NPRS is frequently used scale for quantifying pain. The NPRS is an 11-point scale with anchors of "no pain" and "worst pain imaginable, and it is superior to the visual analog scale in its

simplicity and to the verbal rating scale in its ability to detect change.[67] A 2-point change has been found to be the minimum clinically important difference in patients with low back pain[134] and shoulder pain.[133]

RELIABILITY AND VALIDITY

The methods of measuring the dependent variables have been selected based on their published reliability and validity, and have been addressed earlier in the methodology chapter. GRC, the NPRS, and the ODI are common outcome measures that are used frequently in the clinic. Their clinimetric properties are well established in the literature[52,54,129] and have also been addressed in the previous section of this chapter. Intrarater reliability was calculated for KE (R_1 and R_2), SLR (R_1 and R_2), PPT, and FTF using 10 asymptomatic, healthy volunteers. Measurements were separated by one hour. The mean of 3 trials was recorded and used for analysis.

The intrarater reliability of palpation of spinal landmarks has been proven to be acceptable, where as interrater reliability has a tendency to be lower.[135] In this dissertation study, having only the primary investigator palpate the target segments optimized reliability. In studies that show low interrater reliability, there was no standardization of palpation procedures.[135] Standardization leads to optimal reliability and validity of locating a spinal segment.[135,136] In addition to standardization, using multiple bony landmarks to confirm location also leads to the greatest accuracy for locating lumbar spinous processes.[117] Using only a single bony landmark to determine a spine segment for lumbar epidural injections can lead to treating the incorrect segment up to 50% of the time.[117]

The protocol used by Snider et al[117] in their reliability study was adapted for this dissertation study. A weighted kappa of 0.84 was calculated for accuracy of all experienced

examiners in locating correct spine segments, and the average accuracy was found to be higher than what was achieved by musculoskeletal ultrasound and verified by X-Ray.[117] It is also worth noting that only 1 of 180 segments (<0.6%) identified in the study by Snider et al[117] was more than one vertebral level from the target segment. In this dissertation study DN to T11 or L2 was likely to still have a similar effect on the LE to the thoracolumbar (TL) junction because the SNS output to the LE originates from T10 to L2.[25,26]

THREATS

Many steps were taken to minimize threats to internal and external validity. This dissertation study was prone to selection bias, given that subjects were more likely to participate if they believed DN would help them. Individuals who are opposed to DN or do not think it will help would likely not volunteer. Believing that DN would be helpful could have affected subjects' performances on post-treatment and follow-up testing. Another threat to internal validity was diffusion. Subjects may have known someone who received DN before or had seen it done in the clinic where most of the recruitment took place. Subjects may have been biased based on their comparison to what they observed, or by what a friend or family member had said about their DN experience. Subjects were encouraged not to discuss their experience until after Day 2 in an attempt to mitigate this threat, but this would not account for observations and discussions that occurred prior to Day 1.

Subjects in this dissertation study were randomized to one of two groups in order ensure equal distribution of the demographics between groups. Additionally, this was a double-blind study. The research assistant and all subjects were blinded to group allocation. The primary investigator was blinded to the pre-treatment, post-treatment and follow-up measurements for flexibility and PPT. However the order of testing was not randomized, and the effects of repeated

testing may have improved flexibility measures as the subjects progressed through the study protocol.

Subjects were instructed to refrain from analgesics, caffeine, alcohol and nicotine prior to participation on both days. All of the aforementioned substances are capable of affecting the nervous system, which may confound the results. These recommendations were consistent with similar research protocols investigating SNS activity.[20,86] Subjects were advised not to exercise the days of the experiment because it can affect some indicators of HRV by as much as 74%.[55] Compliance with this recommendation was not monitored, and therefore could not be added as covariates in the analysis.

There were factors that would affect the generalizability of this dissertation study. Subjects were recruited in Montgomery County, Maryland, and one should generalize results to other geographic locations with caution. Only subjects with LBP without radiculopathy and who have no history of lumbar spine surgery were eligible. Therefore, the results cannot be generalized those who have leg pain and to other conditions, including sacroiliac pain, upper back pain, or post-operative LBP. DN was performed at predetermined segments and results should not be generalized to include DN to other spine segments or any other type of manual therapy to the same spine segments. Age limits were predetermined to be 18 to 70 years, inclusive. The results of this dissertation study should not be extrapolated to patients outside this age range.

ETHICAL CONSIDERATIONS AND REVIEW

This dissertation study was reviewed and approved by the Institutional Review Board at Nova Southeastern University. The identifier was 2018-289-Non-NSU-Health. This dissertation study was also registered with ClinicalTrials.gov, and its identifier was NCT03630172.

DATA COLLECTION PROCEDURES

Data collection took place on 2 consecutive days. Subjects were instructed to complete the demographic questionnaire (**Appendix 1)**. The demographic questionnaire included the NPRS and rating scale for needle anxiety. Subjects could also complete the ODI (**Appendix 2)** prior to arrival, but were instructed to not sign informed consent until arriving for data collection. This guaranteed that all questions and concerns were addressed to their satisfaction prior to obtaining consent. Upon arrival to the clinic, potential subjects were screened to ensure they had sufficient hamstring restriction to participate by using the KE test in the same manner it was performed during data collection. If both limbs met the criteria for participation, the most restricted limb was used for analysis. After confirming all inclusion criteria were met and informed consent was obtained (**Appendix 3**), data collection commenced. The methodology for a subject's initial visit has been outlined in **Figure 6**.

Subjects were assigned an alphanumeric code in order to be de-identified on all paperwork associated with this dissertation study. The alphanumeric code was randomly generated on a Random String Generator (http://www.unit-conversion.info/texttools/random-string-generator/). The master list was saved on an external hard drive and stored in a locked cabinet in the primary investigator's locked office. Subjects were randomly assigned to the DN group or the sham DN group. Randomization occurred using a simple method of opaque envelopes sealed with index cards indicating the allocated group inside of it. After a subject was confirmed as eligible, an envelope was selected and opened by the primary investigator. The research assistant took all baseline measurements. These measurements included PPT, FTF test, KE, and SLR, and were recorded on the Participant Results Form (**Appendix 4**).

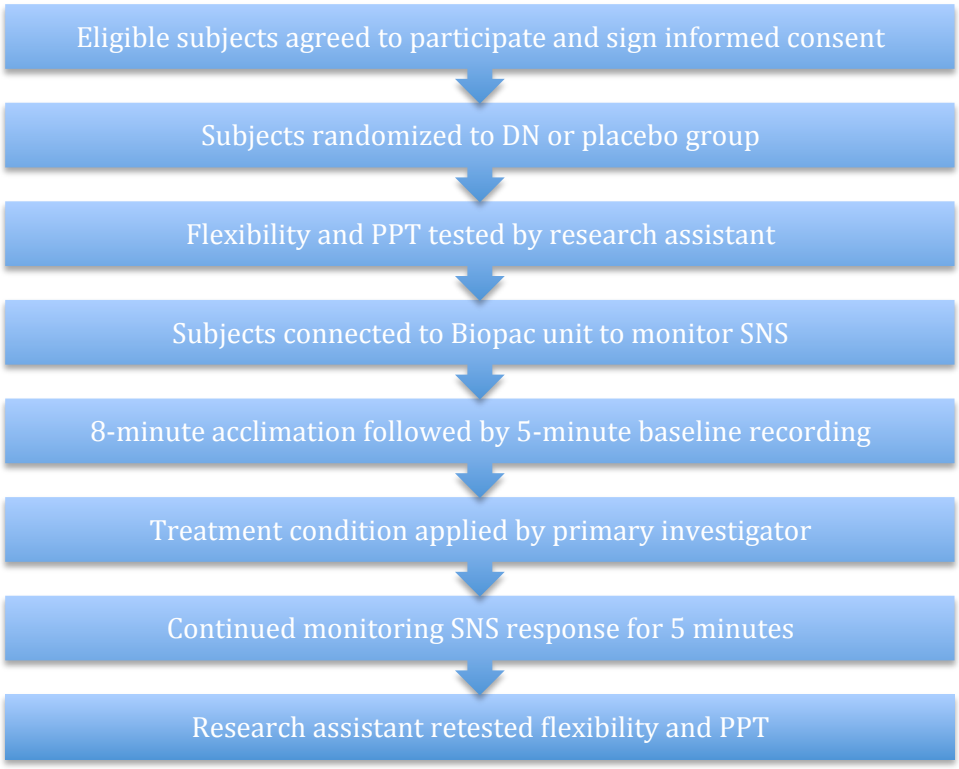

Figure 6. Flowchart for subject's initial encounter.

Fingertip to Floor

The subject was asked to stand without shoes on a 20 cm platform with feet together. While keeping knees, arms, and fingers fully extended, the subject bent forward as far as possible and the vertical distance between the tip of the middle finger and the platform was recorded. In this dissertation study, the score of this test was positive if the subject was able to reach beyond the platform and negative if the subject could not. Distance from the fingertip to the platform was measured in centimeters and the mean of 3 trials was recorded.

Knee Extension

The subject was position in supine on the treatment table, with a small towel roll placed under the lumbar spine. One inclinometer was placed at the midpoint of the femur and was used to maintain 90^{o} hip flexion. A second inclinometer was placed at the midpoint between the tibial tuberosity and the distal end of the tibia. Both were secured with straps. The subject's hip was

flexed to 90 degrees, and then the lower leg was passively extended until the first resistance is felt (R_1). A 1^o margin of error in either direction was allowed for hip flexion. This was performed 3 times and the mean was recorded for analysis. The subject's lower leg was then passively extended until the maximum number of degrees of pain-free knee extension was achieved (R_2). This was performed 3 times and the mean was recorded for analysis. If during either of the R_1 or R_2 measurement the subject was unable to maintain the hip flexed at 90^o the research assistant passively corrected it. The research assistant cued the subject to relax his or her leg if the quadriceps were engaged.

Straight Leg Raise

The inclinometer placed on the thigh was removed while measuring SLR. The subject remained in supine with the towel roll place under the lumbar spine. The ankle remained in a resting position to decrease the effects of neurodynamics.[65,137,138] The subjects were instructed to keep the contralateral limb in contact with the treatment table at all times. The contralateral limb and pelvis were not stabilized, as research has shown that stabilization does not affect SLR reliability measures.[128] The research assistant cued the subject to relax the leg so it could be moved passively, and it was lifted until R_1. The leg was returned to the table and this was repeated 2 additional times. The mean of 3 trials was recorded for analysis. If the research assistant felt like the subject was activating the hip flexors to assist, he cued the subject to relax the weight of the leg. After all trials for R_1 were completed, the subject's leg was then passively moved to R_2. The measurement of R_2 was taken 3 times, and the mean was recorded for analysis.

Pressure Pain Threshold

The towel roll was removed from under the lumbar spine and the subject remained in supine for PPT testing of the UE. A pillow was placed under the dominant arm for support. The

lateral epicondyle was palpated and the algometer was placed upon it. Each subject was instructed to say "stop" when the pressure became "slightly unpleasant pain."[91] Pressure was increased at 0.5kg/sec, and the maximum pressure at the time the subject said "stop" was recorded. The mean of 3 trials was used for analysis.

The subject was then positioned in prone for PPT testing of the hamstrings. Prior to the first measurement, a small "x" was placed on the approximate midpoint of the muscle bellies of the medial and lateral hamstrings to ensure that measurements were taken in the same location every time on both days of data collection. Verbal cues to the subject were identical to those used for the UE. The PPT test was performed 3 times for each of the medial and lateral hamstrings, waiting 30 seconds between trials to minimize the effects of sensitization from repeated stimulation. The means of the 3 trials for each location were recorded for analysis.

Sympathetic Nervous System

Prior to the research assistant collecting data for KE, the skin on the plantar surface was cleaned with an alcohol swab and a 0.5% isotonic saline gel was added to each of 2 disposable Ag-AgCl electrodes. The electrodes were then placed on the plantar surface of the foot. To optimize the EDA signal, the electrodes were in contact with the skin for at least 10 minutes prior to recording. After all baseline measurements were completed, subjects were connected to a BIOPAC® MP36R data acquisition unit (BIOPAC® Systems Inc., Camino Goleta, CA, USA), to monitor HRV, ST, and EDA. The EDA leads were connected to the electrodes on the plantar surface of the foot. The sample rate for EDA was set to 1,000 Hz.[62] A BIOPAC® skin thermistor was fixed with paper tape to the subjects dorsolateral aspect of the foot, approximately 3 cm anterior to the lateral malleolus. The PPG sensor was then fastened to the great toe. A visual representation of sensor placement can be seen in **Figure 7**. Subjects were instructed to avoid

aberrant leg movements in order to minimize signal noise during data collection. Subjects were also advised not to meditate or sleep during recording periods because of the effects on SNS activity.

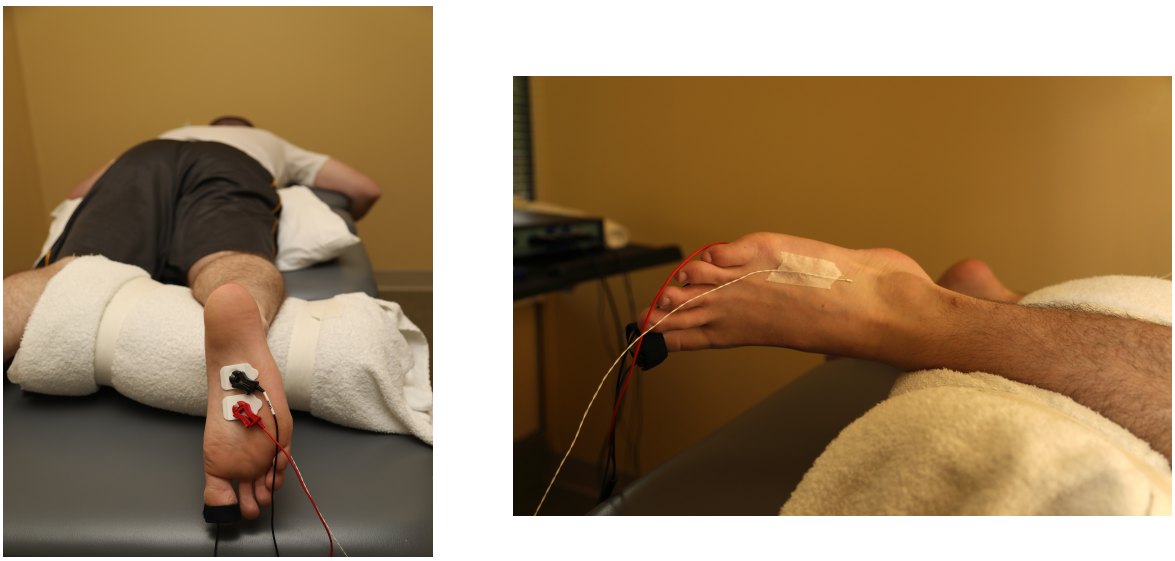

Figure 7. Sensor placement for data collection of SNS outflow.

Following placement of all sensors, T12 and L1 were located using a standardized palpation procedure adapted from the study by Snider et al.[117] On each subject the iliac crests were located, followed by the posterior superior iliac spines. The researcher moved medially to the sacrum and palpated the space between it and the L5 vertebra. Spinous processes were counted superiorly until T12 was reached. The location of T12 was verified by the identification of the 12th ribs as well as comparing the relative size of the T12 and L1 spinous processes (T12 is smaller).[136] The T12 and L1 spinous process were marked with a pen so no additional palpation was required while the subject was being monitored. Proper clean technique was followed for all subjects, including the subjects receiving the placebo. This decreased the likelihood that the subject would know which treatment he or she received. The primary investigator wore gloves, and 70% isopropyl alcohol was used to clean the skin over the muscles that were treated.

An 8-minute acclimation period was allowed for stabilization of all sensors.[20,86] After starting the software, subjects were instructed to inhale deeply. An EDA response within 1 to 2 seconds of a deep inhalation indicated that the subject was a "responder" and that there was good contact with the electrodes. After this was confirmed, the 5-minute baseline recording began. A 5-minute recording was chosen for all recording periods because when analyzing the time and frequency domains for short-term HRV, one must use the same duration for all recordings.[139] The primary investigator then prepared to perform the treatment condition that was randomly assigned.

Dry Needling and Sham Needling

Seiren L-type needles (Seirin Corp., Shizuoka, Japan) were sterile and 0.30 x 60mm in gauge and length. This length was chosen because it would penetrate all layers of erector spinae muscles in subjects with a BMI less than 30 kg/m^2. For the sham DN group, non-penetrating needles were constructed by cutting 100mm needles where the handle meets the shaft, and sanding down any rough edges. Guide tubes from 40mm needles were used to repackage the needles so they appeared the same as the needles for DN. This method of constructing sham needles is an acceptable placebo condition that is indistinguishable from DN in subjects who have never received DN.[140]

Needles were placed using an inferomedial approach. The "safe zone" for the thoracic and lumbar multifidus is between the spinous process and 1 cm lateral, which is approximately one finger width.[141] The needle was inserted perpendicular to the skin and then guided inferiorly and medially until it reached the lamina. Needles were manipulated in a "pistoning" fashion, similar to the "fast-in-fast-out" method popularized by Hong,[9] for 15 seconds. Subjects were

treated on the right and left sides at both segments. All materials were handled according to Occupational Safety and Health Administration Blood Borne Pathogens standards.[142]

After the DN or sham DN had been performed to all segments involved in the treatment protocol, subjects continued to have SNS output monitored to total of 5 minutes. Afterward, a final 5-minute recording was obtained. Subjects were disconnected from the sensors at the conclusion of the final 5-minute recording. The research assistant completed all measurements for FTF, KE, SLR and PPT in the exact manner stated earlier in this chapter.

All subjects attended a follow-up visit 24 hours after their initial visit. The methodology for the follow-up encounter has been outlined in **Figure 8**. In addition to an ODI, subjects completed a questionnaire including the NPRS and GRC at this visit (**Appendix 5)**. The research assistant recorded measurements of FTF, KE, SLR, and PPT of the UE and LE using the same limbs tested on the previous day. Subjects were connected to the BIOPAC® MP36R data acquisition unit as previously described. They underwent an 8-minute acclimation period followed by a 5-minute data collection period. After data collection was complete, the primary investigator revealed a subject's group allocation. Subjects in the sham DN group were offered DN in the same manner as the DN group.

DATA ANALYSES

The data were extracted from the AcqKnowledge software (BIOPAC® Systems Inc., Camino Goleta, CA, USA). A high-pass filter was applied to the PPG raw data to remove any peaks below 0.05 Hz, which may have resulted from movement by the subject during data recording. Prior to conducting the statistical tests, data were analyzed to see if they met the assumptions for each statistical test.

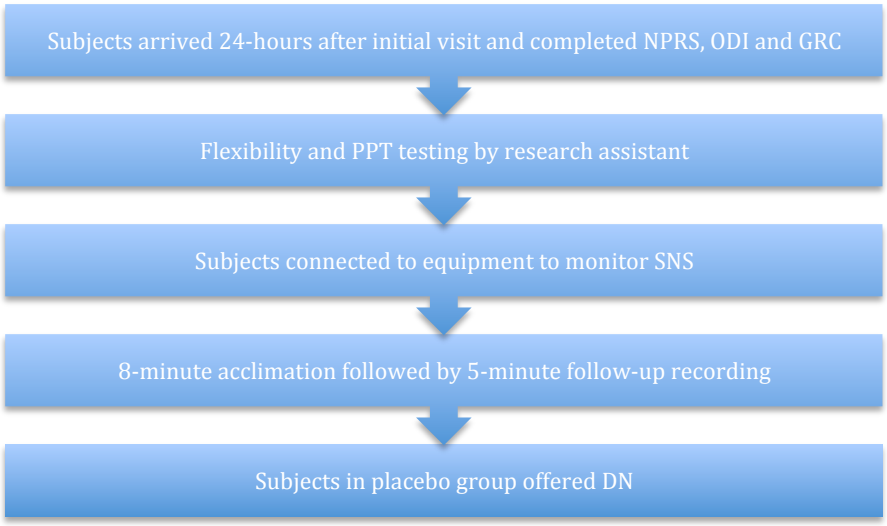

Figure 8. Flowchart for subject's follow-up encounter.

For demographic information, differences in continuous variables were evaluated using *t*-tests. Differences in categorical variables were analyzed using a X^2 test. One-way ANCOVAs were used for each dependent variable (DV) of SNS activity immediately after treatment and at 24-hour follow-up. The independent variable was the treatment condition (DN vs. sham DN). The DVs in this analysis were PPT of the medial hamstring and lateral hamstring, mean tonic EDA, mean ST, LF:HF ratio, rMSSD, and SDPP. The covariates were pre-treatment measurements and self-reported needle anxiety.

One-way ANCOVAs were used to assess between-group differences in local and remote flexibility. The DVs were FTF, KE at R_1 and R_2, and SLR at R_1 and R_2 immediately post-treatment and at 24-hour follow-up. The independent variable was the DN condition. The covariate was the pre-treatment score for the test of interest in each analysis.

Paired *t*-tests were used to calculate differences between UE and LE PPT change score means of the DN group only for baseline and post-treatment as well as baseline and 24-hour follow-up. Pearson's *r* was used to determine if there was a significant relationship between SNS

output, quantified by LF:HF ratio immediately post-treatment, and each of the clinical outcomes measures of GRC, ODI, and NPRS. Statistical significance for all tests was set at $p<.05$.

SUMMARY

This chapter outlined the methodology of this dissertation study. Participants attended 2 consecutive days of data collection, which consisted of flexibility, PPT, and non-invasive SNS testing. This dissertation study was designed to maximize reliability and minimize bias by careful selection of how to measure the DVs. Threats to internal and external validity have been recognized, and how they were mitigated was also discussed. Data management and statistical tests were also addressed.

CHAPTER 4: RESULTS

INTRODUCTION

Fifty-four consecutive subjects with low back pain (LBP) who met the inclusion and exclusion criteria were enrolled in the study and randomly allocated to the dry needling (DN) group (n=27) and sham DN group (n=27) after eligibility was confirmed. This sample included 33 females (61.1%) and 21 males (38.9%). No subjects were lost to attrition and no adverse events occurred. This chapter presents the results of the analyses outlined in the previous chapter. All statistical tests were performed in IBM® SPSS® Statistics for Macintosh, Version 26.0.

RESULTS

Intrarater Reliability

Intraclass correlation coefficient (ICC) values and their 95% confidence intervals were calculated using the means, absolute agreement, and two-way mixed-effects model. The ICC data are presented in **Table 1**.

Table 1. Intrarater Reliability of Research Assistant

Test	ICC	95% Confidence Interval	
		Lower Bound	Upper Bound
FTF	.99	.98	.998
KE R_1	.95	.81	.99
KE R_2	.96	.85	.99
SLR R_1	.97	.90	.99
SLR R_2	.96	.83	.99
PPT	.92	.63	.98

Abbreviations: FTF, fingertip to floor; KE, knee extension; SLR, straight leg raise; PPT, pressure pain threshold.

Descriptive Statistics

Descriptive statistics of each group and *p*-values are presented in **Table 2**. There were no statistical or substantive differences in demographics, Oswestry Disability Index (ODI) at baseline, and numeric pain rating scale (NPRS) at baseline between the DN and sham DN groups.

Hypothesis Testing

Sympathetic Nervous System. Waveforms for sympathetic nervous system (SNS) outflow were visually screened for noise and other aberrant data. One subject's photoplethysmography (PPG) waves were indiscernible. This subject was randomized to the DN group, and therefore the mean of the DN group was used for all HRV statistics for that subject.

Table 2. Baseline Participant Characteristics

	Participants, Mean (SD)		
	DN (n = 27)	**Sham (n = 27)**	***P* Value**
Age, y	38.8 (14.4)	34.5 (11.0)	.23
Female, No. (%)	15 (55.6)	18 (66.7)	.40
BMI	24.5 (3.3)	23.8 (3.0)	.43
Duration of current episode of LBP, d[a]	423.3 (474.2)	476.3 (909.79)	.79
Needle Anxiety (0-10 ordinal scale, with 0 indicating no anxiety with needles)	2.3 (2.3)	1.6 (1.3)	.13
Numeric Pain Rating (0-10 ordinal scale, with 0 indicating no pain and 10 indicating worst pain imaginable)	2.6 (1.3)	2.5 (1.5)	.70
ODI Score (0-100 score, lower scores indicating less disability)	12.6 (7.5)	12.0 (6.7)	.77
Right Hand Dominant, No. (%)	22 (81.5)	25 (92.6)	.22
Right Leg Restricted, No. (%)	14 (51.9)	16 (59.3)	.58

Abbreviations: BMI, body mass index (calculated as weight in kg divided by height in meters squared); ODI, Oswestry Disability Index.

[a] Four missing scores, mean was used for missing values.

Outliers were present in many of the SNS variables. This was expected in a sample of 54 subjects. Dependent variables (DVs) with outliers more than 3 standard deviations from the mean were retested in an ANCOVA with the outliers excluded. In most cases the results were not affected. This will be discussed in the corresponding sections below, if applicable.

Normality was assessed using the Shapiro-Wilk test with a significance level of $p<.05$. Some of the data violated this assumption, however a normal distribution is unlikely with a sample of 54 subjects. Pressure pain threshold (PPT) data post-treatment and at 24-hour follow-up, low frequency to high frequency (LF:HF) ratio of heart rate variability (HRV), electrodermal activity (EDA) data pre-treatment and post-treatment, root means square of the successive differences (rMSSD) post-treatment were not normally distributed. Tests of normality were also significant for standard deviation of peak to peak (SDPP) data with the exception of the DN group at 24-hour follow-up. Because the ANCOVA is robust to violations of normality, the primary investigator proceeded with the analysis.

Scatterplot matrices were used to confirm linearity of the DV and covariates for the ANCOVAs. Pre-treatment scores for all SNS outcomes had linear relationships with post-treatment and 24-hour follow-up measures. Needle anxiety was not linearly related to PPT, EDA, skin temperature (ST), and HRV.

Levene's Test of Equality of Error Variances was used to assess the assumption of equal variances. Alpha level was set to $p<.05$. This assumption was met for all variables at all times except LF:HF ratio post-treatment ($p=.01$), LF:HF ratio at 24-hour follow-up ($p=.047$), rMSSD at 24-hour follow-up ($p=.01$), and SDPP at 24-hour follow-up ($p=.00$).

ANCOVA Results. The adjusted difference values for both groups in all DVs assessed in this hypothesis and their corresponding *p*-values are summarized in **Table 3**. There were no

differences in PPT of the medial and lateral hamstrings post-treatment and at 24-hour follow-up. There was a between-group difference in mean tonic EDA immediately post-treatment, with the DN group having a greater mean EDA, but no difference at 24-hour follow-up. There were no differences in mean ST between groups immediately post-treatment and at 24-hour follow-up.

Table 3. Sympathetic Nervous System Measures for DN and Sham Groups

Measurement	Time	Adjusted Difference (95% CI) DN (n = 27)	Sham (n = 27)	*P* Value
MH PPT (kg/cm^2)	Post-treatment	-0.3 (-1.1, 0.5)	0.3 (-0.5, 1.1)	.51
	Follow-up	-0.2 (-1.2, 0.8)	0.2 (-0.8, 1.2)	.68
LH PPT (kg/cm^2)	Post-treatment	-0.1 (-0.6, 0.9)	0.1 (-0.9, 0.6)	.72
	Follow-up	-0.4 (-1.3, 0.4)	0.4 (-0.4, 1.3)	.32
Mean Tonic EDA (microsiemens)	Post-treatment	1.2 (0.5, 1.9)	-1.2 (-1.9, -0.5)	0.002*
	Follow-up	0.8 (-0.7, 2.3)	-0.8 (-2.3, 0.7)	.28
Mean Temperature (^oC)	Post-treatment	-0.1 (-0.3, 0.2)	0.1 (-0.2, 0.3)	.54
	Follow-up	0.03 (-0.7, 0.8)	-0.02 (-0.8, 0.7)	.94
HRV LF:HF Ratio[a]	Post-treatment	0.36 (-0.16, 0.87)	-0.36 (-0.87, 0.16)	.17
	Follow-up	-0.6 (-1.1, -0.1)	0.6 (0.1, 1.1)	0.02*
HRV rMSSD[a] (ms)	Post-treatment	21.8 (-36.3, 79.9)	-21.8 (-79.9, 36.3)	.46
	Follow-up	-11.0 (-40.6, 18.7)	11.0 (-18.7, 40.7)	.46
HRV SDPP[a] (ms)	Post-treatment	2.7 (-67.4, 72.7)	-2.7 (-72.7, 67.4)	.94
	Follow-up	-101.5 (-197.3, -5.8)	101.5 (5.8, 197.3)	0.04*

Abbreviations: PPT, pressure pain threshold. EDA, electrodermal activity; HRV, heart rate variability; LF:HF, low-frequency to high-frequency; rMSSD, root mean square of successive differences; SDPP, standard deviation of peak to peak intervals.

[a] One subject in the DN group had missing data and the mean of DN group was used.

*Denotes significance $p<.05$

Data for ST were also analyzed including room temperature as a covariate, and the results were not significant immediately post-treatment ($p=.59$) and at 24-hour follow-up ($p=.35$).

There was no difference between groups in LF:HF ratio immediately post-treatment. At 24-hour follow-up the difference in LF:HF ratio was significant, with the DN group having a lower ratio. There was one outlier in the sham group that had a Z-score greater than 5.0 at 24-hour follow-up. Because this outlier was extreme and may not be representative of the sample, the analysis was also performed again with this case excluded. After excluding the outlier, Levene's Test of Equality of Error Variances test was no longer significant (p=.11) and the between-group difference was still significant (p=.02) at 24-hour follow-up, with the DN group having a lower LF:HF ratio. There were no differences in rMSSD between the groups at post-treatment and 24-hour follow-up. There was no difference in SDPP between the DN and sham groups immediately post-treatment. There was a difference in SDPP at 24-hour follow-up between the DN and sham groups, with the DN having a lower SDPP.

Flexibility. Outliers existed in the KE and SLR data, but not in FTF data. Normal distributions were not present across all variables, however because the ANCOVA is robust to violations of normality, the primary investigator continued with the analysis. Levene's Test of Equality of Error Variances was not significant for all tests of flexibility (p>.05). Linearity was assessed using scatterplot matrices. Linear relationships between the covariate and DVs existed for all flexibility tests in both the DN and sham groups.

ANCOVA Results. The adjusted difference values for both groups and corresponding p-values are summarized in **Table 4**. There was a significant difference in immediate change in local flexibility favoring the DN group ($F_{1, 51}$ = 4.047). There was no difference between groups at 24-hour follow-up ($F_{1, 51}$ = 1.038). All remote flexibility tests at R_1 and R_2 did not differ between groups immediately post-treatment (KE R_1: $F_{1, 51}$ = .429; KE R_2: $F_{1, 51}$ = 1.394; SLR

R_1: $F_{1, 51}$ = .258; SLR R_2: $F_{1, 51}$ = 1.790) and at 24-hour follow-up (KE R_1: $F_{1, 51}$ = .215; KE R_2: $F_{1, 51}$ = .397; SLR R_1: $F_{1, 51}$ = .065; SLR R_2: $F_{1, 51}$ = 3.457).

Table 4. Local and Remote Flexibility Measures for DN and Sham Groups

Measurement	Time	Adjusted Difference (95% CI) DN (n = 27)	Sham (n = 27)	*P* Value
Local Flexibility (cm)				
FTF	Post-treatment	1.2 (.002, 2.3)	-1.2 (-2.3, -.002)	0.0495*
FTF	Follow-up	0.9 (-0.9, 2.6)	-0.9 (-2.6, 0.8)	.31
Remote Flexibility (degrees)				
Knee Extension R_1	Post-treatment	0.8 (-1.7, 3.3)	-0.8 (-3.3, 1.7)	.52
Knee Extension R_1	Follow-up	0.6 (-1.9, 3.0)	-0.6 (-3.0, 1.9)	.65
Knee Extension R_2	Post-treatment	-1.5 (-4.1, 1.1)	1.5 (-1.1, 4.1)	.24
Knee Extension R_2	Follow-up	1.0 (-2.1, 4.0)	-1.0 (-4.0, 2.1)	.53
Straight Leg Raise R_1	Post-treatment	0.5 (-1.5, 2.5)	-0.5 (-2.5, 1.5)	.61
Straight Leg Raise R_1	Follow-up	0.3 (- 2.5, 1.9)	-0.3 (-1.9, 2.5)	.80
Straight Leg Raise R_2	Post-treatment	1.5 (-0.8, 3.8)	-1.5 (-3.8, 0.8)	.19
Straight Leg Raise R_2	Follow-up	-1.8 (-3.7, 0.1)	1.8 (-0.1, 3.7)	.07

Abbreviations: FTF, fingertip to floor.
*Denotes significance $p<.05$

Segmental Effects of Dry Needling. Pre-analysis data screening showed all but two of the PPT variables met the assumption of normality. Because the *t*-test is robust to violations of normality, the primary investigator continued with the analysis. Mean differences between the lower extremity (LE) PPT and the upper extremity (UE) PPT from baseline to post-treatment and baseline to 24-hour follow-up are summarized in **Table 5**. There was no difference in PPT change scores for the UE and medial hamstrings immediately post-treatment and at 24-hour

follow-up in the DN group. There was no difference in PPT change scores for the UE and lateral hamstrings immediately post-treatment and at 24-hour follow-up in the DN group.

Table 5. Summary of PPT[a] Mean Differences from UE in DN Group (n=27)

	Mean Difference (95% CI)	*t* value	*P* Value
Medial Hamstrings[b]			
Post-treatment	0.1 (-0.7, 0.9)	-0.253	.80
24-hr follow-up	-0.07 (-0.9, 0.7)	-0.191	.85
Lateral Hamstrings[b]			
Post-treatment	0.2 (-0.6, 1.0)	0.523	.61
24-hr follow-up	0.4 (-0.4, 1.1)	1.035	.31

[a] PPT, pressure pain threshold (measured in kg/cm^2).
[b] tested subject's most restricted limb, mean of three trials.

Heart Rate Variability and Clinical Outcomes. The normality assumption was violated for all variables (p=.00), however because Pearson's r is robust to violations of normality the primary investigator proceeded with the analysis. In the DN group, one subject's PPG waves were indiscernible, and therefore the mean of LF:HF ratio for the DN group was used for that subject.

Means, standard deviations, r values and p values for the four variables included in this analysis are listed in **Table 6**. The analysis showed that there is no correlation between LF:HF ratio of HRV immediately post-treatment and GRC scores, ODI scores at 24-hour follow-up, and NPRS scores at 24-hour follow-up.

Table 6. Descriptive Statistics for Correlation Variables

Measurement	All Subjects (n = 54) 24-hour Follow-up Mean (SD)	*r* value	*P* value
HRV LF:HF	1.29 (1.00)	---	---
Numeric Pain Rating (0-10 scale, higher scores indicate higher pain rating)	1.8 (1.5)	0.218	.11
ODI score (0-100 scale, higher scores indicate higher self-reported disability	9.6 (7.7)	-0.173	.21
GRC (-5 to 5, with 0 meaning no change, positive numbers indicate improvement and negative numbers indicate decline)	0.6 (1.1)	0.171	.22

Abbreviations: HRV, heart rate variability; LF, low frequency. HF, high frequency. ODI, Oswestry Disability Index; GRC, Global Rating of Change.

SUMMARY

This chapter presented the results from the statistical tests that were chosen a priori to answer the research questions for this dissertation study. There were significant differences in EDA activity immediately post-treatment, with the DN group having a greater mean EDA after adjustment of pre-treatment scores. The HRV data for LF:HF ratio and SDPP were significant at 24-hour follow-up, however the sympathetic activity was not correlated with clinical outcomes 24-hours after treatment. Only local flexibility was significantly different between the two groups immediately post-treatment. The results of PPT testing did not support the hypothesis of segmental effects of DN.

CHAPTER 4: DISCUSSION

INTRODUCTION

The chapter presents the discussion of the findings outlined in the previous chapter, and relates them to prior studies. The limitations of the methodology in this dissertation study are addressed, and the implications for practice and for future research are also discussed.

DISCUSSION AND INTERPRETATION OF RESULTS

Sympathetic Nervous System Outflow after Dry Needling

Based on the initial review of literature, the expected findings were an increase in pressure pain threshold (PPT), an increase mean tonic electrodermal activity (EDA), a decrease in mean skin temperature (ST), an increase in low frequency to high frequency (LF:HF) ratio of heart rate variability (HRV), and a decrease in root mean square of successive differences (rMSSD) and standard deviation of peak to peak intervals (SDPP) measures of HRV immediately post-treatment and at 24-hour follow-up. Changes in this manner would have supported an increase in sympathetic outflow after dry needling (DN). Multiple dependent variables (DVs) that receive input from the sympathetic nervous system (SNS) were included in this hypothesis in order to provide greater evidence of SNS activation if there was significance across all DVs, which theoretically should have occurred.[96] Most of the DVs in this hypothesis did not respond as expected, and this phenomenon has been observed previously.[143]

Pressure Pain Threshold. One's perception of pain is affected by local, peripheral, spinal and supraspinal structures.[72] These processes are complex and not fully understood. The thoracolumbar (TL) junction is segmentally linked to the lower extremities (LEs) by the sympathetic ganglia, and stimulation of the sympathetic ganglia is capable of producing a profound analgesic effect. EDA confirmed sympathetic activation in the DN group only

immediately post-treatment. The expected difference in PPT of the LEs between the DN and sham groups that would be associated with an increase in EDA did not occur.

To better understand the results in this dissertation study, mean change scores were calculated and compared beyond the presence of statistical significance. Both groups experienced an increase in PPT at the medial hamstrings immediately post-treatment, with continuing increase at 24-hour follow-up. For the lateral hamstrings, both groups experienced an increase in PPT immediately post-treatment. However, only the sham group experienced an increase at 24-hour follow-up. The DN group mean at 24-hour follow-up appears to have reverted back to baseline. This trend has not been observed in the previous literature on hypoalgesia after DN.

Evidence of segmental or remote hypoalgesia can be found in the literature.[29,50,77,93] The studies that have shown segmental increases in PPT were observed in muscles that were myotomally connected to the muscle being treated.[50,93] In this dissertation study, there was no myotomal connection between the TL junction and hamstrings. Some of the studies finding segmental or widespread PPT differences compared the DN group to a no-treatment control group.[29,77] Including a no-treatment control group allows for comparison of the natural course of the condition, however expectation of positive results may have been a factor in the significant findings in these studies. Alternatively, Chou et al found a modest increase in local PPT after sham DN, however the percent change in the sham group did not surpass the two DN treatment groups.[30]

Substance P is a pro-nociceptive neuropeptide that is involved in the transmission of pain peripherally and through the central nervous system. Hsieh et al observed suppression of substance P in the lumbar region of the spinal cord after DN to the gastrocnemius in rabbits.[144]

Suppression of substance P implies a hypoalgesic effect of DN, though it was not possible to test PPT in their study.

Mean change scores from baseline for both groups were positive, indicating some effect on pain modulation, but mean change scores did not surpass the minimum detectable change (MDC) and minimum clinically important difference (MCID) for PPT in the LE.[91,145] This could mean that the changes in PPT were a result of measurement error and may not reflect clinically meaningful improvements in pain modulation after DN to the TL junction. The 95% CIs for all LE PPT data were also compared to the MDC and MCID for the LE that have been calculated in other studies.[91,145,146] In this dissertation study, 6 of the 8 change scores in the LE among both groups had a 95% confidence interval that included the MCID calculated by Jorgesen et al in subjects with chronic pain.[145] MCID results should be interpreted with caution because the cut-off points used to dichotomize subjects who do or do not improve on a particular construct can be arbitrary, and MCID results can vary widely based on which of the 9 methods was used for calculation.[147,148]

In this dissertation study, changes in PPT in the sham group may have resulted from the sham DN not being fully inert. Functional magnetic resonance imaging has shown that placebo hypoalgesia results from activation of supraspinal structures that inhibit descending pain messaging.[149] Changes observed in the sham group in this dissertation study were often greater than the DN group. This phenomenon has been observed in another DN study.[28] Huguenin et al observed a greater decrease in pain rating after sham DN when compared with the active DN group, but the between group differences were not significant.[28] Tekin et al observed a significant immediate decrease in pain rating scores after sham DN to the neck in subjects with myofascial pain syndrome.[39] Tekin et al[39] used a non-penetrating sham needle similar to this

dissertation study, and theorized that their sham needle simulated cutaneous afferents to provide a weak hypoalgesic effect. Stimulation of cutaneous afferents can elicit a SNS effect that may have been strong enough to make the between-group differences insignificant in this dissertation study.[150] Ceccherelli et al[151] hypothesized that muscular afferents may be more important than cutaneous afferents in the hypoalgesic response, and muscular afferents may have been stimulated in this dissertation study by manual compression of the muscles prior to performing the sham DN. Including a no-treatment control group would have allowed for comparison of the placebo hypoalgesia observed in this dissertation study.

PPT testing to the LEs in this dissertation study was part of a larger protocol that included PPT to the upper extremity (UE). Testing was performed in the same order for all subjects at baseline, post-treatment and 24-hour follow up. One cannot ignore the possible effects of temporal summation, which are more likely to occur in individuals with chronic pain because of diminished pain inhibition.[152] Temporal summation refers to a decrease in pain threshold after repeated stimulation secondary to increasing excitability of the dorsal horn in the spinal cord.[72] Repetitive stimulation in one with chronic pain may cause amplification of the pain message.[153] The research assistant observed a progressive decrease in PPT scores with repeated testing, which may have been caused increasing dorsal horn excitability, and this observation should be considered when interpreting the results.

Electrodermal Activity. EDA is the best indicator of SNS activity because it receives no input from the parasympathetic nervous system (PNS), unlike other measures that have been included in studies of the autonomic nervous system (ANS).[62,96] Because of the very limited number of studies on the effect of DN on EDA, this discussion will include EDA response to other manual therapies. There was a significant between-group difference in mean tonic EDA

immediately post-treatment. Only the DN group experienced an increase in EDA immediately post-treatment, indicating sympatho-excitation was exclusive to DN. The 95% CI upper and lower bounds were positive, therefore one can be reasonably certain an increase in EDA would occur in the population represented by this sample. The change in mean tonic EDA and its 95% CI upper and lower bounds were negative for the sham group post-treatment. A decrease in EDA is a common observation in subjects at rest[96] and has been seen in placebo and control groups in a previous studies.[13,20]

The observed mean percentage change in the DN group on Day 1 of this dissertation study was 13.4% (SD=23.0%), which was lower than previously observed percentages of change in SNS activity with joint mobilization[15-17,85] and of similar magnitude to other studies.[13,20] The studies that observed greater increases in EDA included 3 bouts of joint mobilization that were 1 minute in duration, which is a greater overall treatment volume than this dissertation study.[15-17] The lower SNS response is likely explained by the lower treatment volume because an SNS response occurs in direct proportion to the stimulation.[36] No MCID has been published for EDA[88] so it cannot be determined if the observed 13.4% increase in tonic EDA is clinically significant.

There was no between-group difference in mean tonic EDA at 24-hour follow-up, and this may be attributed to one of several reasons. Some experts propose a daily variation in EDA within an individual,[62,154] however another confirms minimal variation and good test-retest reliability coefficients ranging from 0.50 to 0.70.[96] Other studies have shown similar transient results of ANS activation with DN[155] and joint mobilization.[98] Sillevis et al used pupil diameter to measure SNS activity and found the sympatho-excitatory effect of DN to last approximately 20 minutes, at which time the pupil started approaching its pre-treatment diameter.[155] La Touche

et al found that cervical mobilization resulted in changes in EDA, respiration rate and heart rate. These changes were significant immediately after treatment but returned to baseline at short-term follow-up.[98] Finally, it is believed that the initial sympatho-excitation from manual therapy can become sympatho-inhibition as quickly as 20 minutes after treatment, and it is unclear how long it lasts or if it occurs in all subjects after manual therapy.[74] It is possible that the lack of significance between the two groups at 24-hour follow-up could be attributed to some subjects in the DN group experiencing sympatho-inhibition after initial sympatho-excitation.

There are two aspects of EDA that could have been used in analysis; this dissertation study used mean tonic EDA rather than phasic EDA. Tonic EDA is a slower-acting signal detected at rest and is indicative of general autonomic arousal.[62] Tonic EDA was the appropriate choice of measurement at rest in the absence of stimuli during each 5-minute recording.[156] Phasic EDA refers to the rapid changes, or skin conductance responses (SCRs), that occur spontaneously or in response to stimulus. It is used more frequently in research, however it represents only a small portion of overall EDA and should be interpreted with caution.[62] Tonic EDA is sometimes considered a flawed measure because there can be day-to-day variations in one's EDA and because it includes SCRs, which will inflate the mean tonic EDA value.[62] In other words, mean tonic EDA would include some data from phasic EDA.[62]

Phasic measures, specifically SCRs and their amplitudes, offer additional information about SNS activity but are also not without methodological concerns.[62,94] When analyzing SCRs it is difficult to determine if they are spontaneous or event-related. Phasic values were extracted from the data but were not included in the analysis for this dissertation study because they were not part of the initial hypotheses. Visual examination of the data showed more SCRs during treatment when compared with pre-treatment and post-treatment data. Phasic EDA confounding

the values of tonic EDA would have been more likely to occur if data were collected during the treatment phase of the experiment when phasic responses were greatest in number.

The results of this dissertation study conflicted with the results of other DN studies that have used EDA as an outcome for SNS activity post-treatment. Two recent studies have shown a down-regulation of the SNS.[22,23] Both of these studies treated myofascial trigger points (MTrPs) in the upper trapezius (UT), and it has been proposed that treatment in the cervical spine results in suppression of the SNS, while treatment in the thoracic spine results in excitation because its proximity to the sympathetic ganglia.[157-160] The discrepancy between the results of this dissertation study and other studies may be a result of those studies using a higher treatment volume or using phasic measures of EDA, which captures only a small percentage of overall EDA. Tonic and phasic EDA changes are associated with activity in different areas within the brain.[161] Tonic EDA changes correlate negatively with brain activity in the ventromedial prefrontal cortex and orbitofrontal cortex, where as phasic EDA changes were associated with brain activity in the dorsal anterior cingulate cortex, insular cortices, thalamus, hypothalamus and lateral prefrontal cortex.[161]

To date, very few studies have used EDA as an indicator of increased SNS activity after DN.[22,23] Increased EDA immediately after other forms of manual therapy has been seen in previous studies.[13,15,20,88,162] Jowsey and Perry[13] found that postero-anterior glides to T4 were sympatho-excitatory, and this effect was observed in the hands. The area treated by Jowsey and Perry[13] is responsible for sympathetic outflow to the upper extremities (UEs), but the authors did not include testing of LE to determine if the effects were segmental and extra-segmental. Chu and colleagues[88] did a systematic review of the literature on manual therapy of the cervical and thoracic spine and found a peripheral sympatho-excitatory effect measured by EDA. The effect

size was small to moderate, and the authors questioned the clinical relevance of the data because of the lack of long-term follow-up in the studies they reviewed. Some of the studies included in the review used asymptomatic healthy subjects and did not include additional data collection beyond immediate follow-up.[13,15,16,20] In the lumbar spine, Moutzouri and colleagues[20] used a mobilization to facilitate flexion while monitoring SNS outflow via EDA. They found a transient sympatho-excitatory response dermatomally which was significantly greater than the control group, but not the placebo group.

While the results of this dissertation study favor an increase in SNS activity, it does not give information on if the effect is regional or extra-segmental. The spine segments associated with sympathetic outflow to the LEs are T10 to L2,[26] and increased EDA was detected in the foot in this dissertation study. A way to determine if the effects are extra-segmental would be to simultaneously test the UE and LE after DN. Quantifying EDA of the UE and LE simultaneously would allow for comparison of segmental and extra-segmental changes, which would aid in understanding if specific techniques are needed to address a body part or region, or if the effect is global. A similar methodology has been seen in DN studies using PPT as an indicator of segmental and extra-segmental effects for hypoalgesia.[30,163]

Skin Temperature. The results of this dissertation study showed that sympathetically-mediated vasoconstriction was not greater in the DN group when applied to the TL junction. This was observed immediately post-treatment and at 24-hour follow-up. Co-activation of vasomotor and sudomotor sympathetic neurons occur together frequently,[95,96] so the lack of significance of ST changes immediately post-treatment was not expected given that there was a between-group difference in EDA. The presence of sudomotor changes without vasomotor changes has been observed in joint mobilization studies.[85,86] ST can be influenced by a subject's environment

because extremity blood flow is affected by ambient temperature.[164] Ambient temperature was controlled and recorded during this dissertation study. The results of the ANCOVA did not change when ambient temperature was added as a covariate. Both the DN and sham DN groups experienced a degree of vasoconstriction immediately post-treatment given that the change scores for mean ST and the upper and lower bounds of the 95% CIs were negative for both groups. Both DN and placebo needling are believed to activate the periaqueductal gray in the brain,[10] which is responsible for thermoregulation, which includes skin blood flow.

Further examination of change scores revealed an increase in ST of the DN group at 24-hour follow-up, however the difference between groups was not significant. There are two studies that used ST as an outcome variable to measure the remote sympathetic effects of DN and the results of these studies are conflicting.[40,165] Skorupska et al used infrared thermovision rather than the skin thermistor used in this dissertation study. The authors found a significant increase in ST in the area of referred pain and a small decrease in skin temperature of the foot, which was outside the area of referred pain for the muscle that was treated.[40] Seixas et al found no significant change in ST in local and remote areas after DN, however it should be noted that their study included only 5 subjects and no placebo or control group for comparison.[165] In this dissertation study, the thermistor was not placed in the area of referred pain for the T12 and L1 multifidi. Like the subjects in the study by Skorupska et al,[40] subjects in the DN group of this dissertation study experienced a greater, albeit statistically insignificant decrease in ST outside of the area of referred pain. Sandberg et al[166] investigated local effects of DN on skin blood flow using a different form of photoplethysmography (PPG) than was used in this dissertation study for analysis of HRV. They found superficial vasodilation locally in healthy subjects more so than subjects with chronic neck pain. The authors did not include a remote location in their

methodology. They attribute these local changes to local vasodilative substances, such as calcitonin gene related peptide (CGRP), overriding the effects of noradrenaline and neuropeptide Y, which are vasoconstrictors. The release of CGRP happens in greater concentration locally, which could explain why local vasodilation and peripheral vasoconstriction have been observed concomitantly in other studies.[40,166]

Because of the limited number of studies of how DN affects ST, the literature review included other forms of manual therapy. Studies using ST as a DV after mobilization or manipulation have also showed mixed results.[15,17,85-87,98,162] Some of the studies that found significance used healthy, asymptomatic subjects and the results may not be generalizable to a clinical population.[15,85] Another study using joint mobilization on a clinical population did not find significance (p>.05), however it included subjects with chronic pain.[98] Subjects in this dissertation study had a mean duration of pain that would be classified as chronic, and there can be sympathetic changes that occur in the presence of chronic pain that could confound the results for changes in ST.[167]

A previous systematic review of 11 articles focused on the sympathetic effects of manual therapy, specifically manipulation and mobilization to the cervical and thoracic spine. The combined analysis showed a moderate to large effect of manual therapy to the cervical and thoracic spine on ST.[88] Vicenzino et al found mixed results in ST changes after manual therapy.[162] Hand and elbow temperature were monitored in their study and only the hand experienced a significant change. The authors stated in their discussion that pileous skin, such as the area of testing in this dissertation study, may not be as sensitive to SNS changes.[162] Blood flow is regulated by arteriovenous anastomoses, which are sympathetically innervated and most prevalent in hairless skin.[123] Chiu et al[15] also did not find significant between-group differences

in ST in their study, but they did not specify where sensors were placed. Other studies placed the thermistor on hairless skin and found no difference between manual therapy and a placebo[17,86,98] or control group,[86] however there was evidence of vasoconstriction because ST decreased after each session of manual therapy. Most studies finding no between-group difference in ST compared with placebo did not direct the manual therapy to the part of the spine responsible for sympathetic outflow to the tested limb.[15,86,98] Placing the thermistor on hairless skin in this dissertation study, such as the sole of the foot, may have yielded a significant result and this should be considered in future studies.

Studies that found a decrease in ST used a treatment dosage of joint or soft tissue mobilization that was greater than the volume of this dissertation study.[17,162,168] In this dissertation study 4 points were treated for approximately 15 seconds, totaling 1 minute of active treatment. The most common joint mobilization protocol was 3 x 1 minute with 30 seconds to 1 minute rest between bouts, but was as high as 3 x 2 minutes.[88] Bayo-Tallon et al found a decrease in ST after 25 minutes of manual therapy provided to healthy children.[168] Because the strength of the SNS response to DN is directly proportionate to the strength of the stimulation,[36] a greater treatment volume may be required to see the expected outcome of significant vasoconstriction.

Vicenzino et al[162] argued that maximum ST was a superior indicator of SNS activity and used it, rather than mean ST, as a DV in their study on the sympathetic effects of manual therapy. Further investigation of the data in this dissertation study using the maximum ST showed that the DN group had a significantly lower maximum ST immediately post-treatment (p=.04), after controlling for pre-intervention values and needle anxiety, with a medium effect size (η^2_p=.10).[169] At 24-hour follow-up there were no between-group differences in maximum ST

(p=.30). This should not be considered a significant finding of this dissertation study given that maximum ST was not chosen a priori as a DV, but maximum ST should be considered as a DV in future studies.

Heart Rate Variability. The HRV findings conflicted with the EDA findings in this dissertation study. Significant between-group differences in EDA immediately after treatment indicated increased SNS activity, but the same phenomenon was not reflected in HRV values. At 24-hour follow-up there were significant findings in HRV, while neither EDA nor ST showed the expected corresponding changes. SDPP at 24-hour follow-up in the DN group was lower, indicating increased SNS activity or decreased PNS activity. The LF:HF ratio in the DN group was lower at 24-hour follow-up, indicating lower SNS activity relative to PNS activity. The two significant findings for HRV appear to be conflicting, but further investigation of how the SNS and PNS influence different metrics of HRV may explain the observed occurrence.

HRV is dependent upon control from both the SNS and PNS, and it is not as simple as a "give and take" inverse relationship. The SNS can suppress PNS activity, but at times the PNS activity can increase in response to an increase in SNS activity.[80] The assumed linear relationship between the two parts of the ANS does not exist.[170,171] The mechanisms that govern the SNS and PNS effects on cardiac rhythms remain unclear. Both PNS and SNS blockade can affect low frequency (LF) rhythms by up to 75%, and this fact should be considered as a reason for inconsistency in HRV responses involving the LF bands.[171] Change in rMSSD are more highly influenced by the PNS,[80,157] and changes in SDPP can be mediated by both the SNS and PNS.[157] LF spectral power is used in the literature to reflect SNS changes, but up to 50% of the variability in LF spectral power can be attributed to the PNS.[80] While LF:HF ratio is a common DV in HRV studies,[19,158,168,172-174] the results should be interpreted with caution because of how

both branches of the ANS affect LF values. Ultimately, the lower SDPP values in the DN group at 24-hour follow-up may have been a result of PNS withdrawal and not SNS activation. This is substantiated by the lack of significant change in EDA at 24-hour follow-up, which is purely sympathetic.

Any stimulation of cutaneous afferents can induce changes in heart rate (HR), which would influence HRV.[150] Palpation to identify T12 and L1 was performed prior to starting baseline recording, so this was a minimal but consistent factor in the values obtained across all subjects during recording. It is possible that sham DN in addition to palpation of the spinous processes and compression of the muscles around the sham needle was enough to influence HRV during Day 1 recording. Mechanical pressure on skeletal muscles had varying effects on HR responses in rats. Changes in HR were negatively correlated with the pre-stimulus HRs.[150] If this is also true in humans, pre-intervention HRs may have been an appropriate covariate and should be considered in future studies. HR data were collected but were not part of the analysis in this dissertation study because it was not declared as a covariate a priori.

At the time of writing this discussion, the only studies of the effect of needling therapies on HRV were acupuncture studies. Some studies on the autonomic effects of other forms of manual therapy have used HRV as an outcome variable, though it is still not a common outcome variable for physical therapy research.[175] The results of the available manual therapy studies have been contradictory. A pilot study of 11 subjects showed immediate changes in 1 of 3 time domains, but no change was present at 24-hour follow-up for both time and frequency domains.[176] Another study on children showed that manual therapy can affect the PNS for up to three weeks post-treatment.[168] Additionally, some of the studies of manual therapy that included HRV as a DV had small sample sizes[19,159,172,173] or used asymptomatic subjects.[19,168,174] These

studies should be viewed as preliminary findings to inspire larger studies with a clinical population.[159,173]

Compiling the results of the available studies using HRV, there appears to be a trend toward the effect on the ANS being dependent upon the region where the manual therapy is directed. Manual therapy techniques directed toward the cervical spine trend toward having an effect on the PNS, as indicated by an increase in HRV time domain values and some frequency domain values. The authors attributed this to the proximity of the treated area to the vagus nerve.[168,175,176] Alternatively, manual therapy techniques directed toward the thoracic spine trend toward affecting the SNS, as indicated by a decrease in HRV time domain values and some frequency domain values. The authors of these studies attributed these changes to the proximity of the treatment to the sympathetic ganglia.[158-160] A recent systematic review of the literature regarding HRV and manual therapy reached a similar conclusion.[157] Two studies[177,178] that observed the inverse of the aforementioned phenomenon did not appear to control for pre-intervention scores in their analyses, and this may have resulted in erroneous conclusions.

The HRV values in this dissertation study for rMSSD and SDPP were substantially higher when compared with normative values.[179] The LF:HF ratio in this dissertation study was closer to normative data.[179] The study establishing normative data included over 21,000 healthy adults over 40 years of age. It is known that PNS activity decreases with age, which would lower values of normative data in time domains specifically.[80] This may explain why the sample in this dissertation study was higher. There is also a 6% difference in PPG measures of HRV when compared with electrocardiogram (ECG), and this may also explain in part why the sample in this dissertation study differed from normative values established from ECG data.[80]

There are many factors that can influence HRV. Respiration rate could explain some of the variability in HRV data, specifically high frequency (HF) band and rMSSD values because they are more parasympathetically-mediated.[80] Two methods that have been used previously to limit the effect of respiration rate on HRV is to either control for breathing rates in the analysis or to have subjects breathe at a specific rate. Respiration rate was not recorded or standardized in this dissertation study, and this may have introduced some error into the HRV data. Other factors can influence HRV, including but not limited to heart rate, physical fitness, biological sex, stress and age.[80] Age, heart rate and biological sex data were gathered but were not covariates in the analysis, in accordance with the a priori hypotheses. Physical fitness and stress beyond general needling anxiety were not quantified but should be considered as covariates in future studies involving HRV.

The lack of significant findings immediately post-treatment may be explained by changes in HRV possibly occurring very quickly and then reverting to baseline before the post-treatment recording began. Berntson et al[171] recommended 1 to 2 minute recordings at critical points in a treatment protocol in order to capture enough data to derive the time and frequency domain metrics. Other experts report 5-minute recordings to be optimal for short-term HRV analysis,[139] and therefore each segment of the experiment lasted 5 minutes, including the treatment segment which was not used in the analysis. The treatment procedure lasted 90 seconds at most, allowing for 3.5 minutes of HRV changes that were not part of the analysis in this dissertation study. The clinical relevance of such transient changes is questionable, however future research may include multiple 1 to 2 minute recordings at varying post-treatment intervals.

Because of the many factors influencing HRV, a larger number of subjects should have been included to mitigate the variability. The power analysis for this dissertation study used PPT,

not HRV, to determine sample size because of the lack of DN studies that used HRV as an outcome variable. A post hoc power analysis was performed using G*Power, and power was calculated as 0.30. Based on the data collected, G*Power was also used to calculate the required sample size to detect significant differences in the LF:HF ratio data using the one-way ANCOVA with an alpha level of .05 and a power of 0.8. It determined that a total of 201 subjects would be required. Thus, the sample size in this dissertation study was too small to achieve adequate statistical power for HRV.

Local and Remote Flexibility Outcomes after Dry Needling

Based on the initial review of the literature, the expected findings were a greater increase in local and remote flexibility in the DN group. The results of this dissertation study supported the changes in local flexibility that were hypothesized, but not remote flexibility.

Local Flexibility. The results of this dissertation study showed an immediate local change in flexibility after DN, with a medium effect size (η^2_p=.07).[169] One possible explanation for the observed increase in local flexibility is attenuation of alpha motoneuron excitability. Various forms of manual therapy have been found to decrease the Hoffmann reflex (H reflex), which indicates diminished alpha motoneuron excitability in the area that was treated,[180] or an area that was segmentally-related to the area treated.[181] This effect was transient.[180,181] Previous studies have shown that the H reflex diminished from 30 seconds[181] to 1 hour[180] after intervention, and fingertip to floor (FTF) was retested in that window of time.

A second possible explanation for the increase in local flexibility is a decrease in spontaneous electrical activity within the muscle. A reduction in endplate noise has been seen after DN in human[182,183] and animal[78,184] studies, even if the DN is not aimed at an active MTrP.[184] Endplate noise is associated with an excess of acetylcholine at the neuromuscular

junction, facilitating the formation of MTrPs, which decreases the extensibility of a muscle. The reduction in endplate noise is thought to be a consequence of decreased acetylcholine and increased acetylcholinesterase.[184]

A third possible explanation is the mechanical effects of the needle on the MTrP. It has been postulated that a MTrP results from a high degree of overlap between actin and myosin filaments in the sarcomere. DN may cause a local stretch to the contracted muscle, which would reduce the amount of overlap of actin and myosin allowing the muscle to fully lengthen.[6] Mechanical stimulation by a needle on muscle fibers has also been shown to reorganize collagen fibers into a more parallel formation, although it is seen more commonly in needle rotation techniques, which were not employed in this dissertation study.[185]

Many studies have looked at the immediate effects of DN on flexibility.[27,163,186-190] Fewer have included information on a longer duration for short-term follow-up.[188,191] Ceballos-Laita et al[187] found a significant improvement and large effect size in range of motion (ROM) after 3 sessions of DN to hip muscles. The larger effect size in their study may be attributed to the area of treatment being determined by examination of the subject. In this dissertation study the treatment area was predetermined and an individualized approach may have resulted in a larger effect size. Alternatively, Campa-Moran et al[188] observed a small and statistically insignificant increase in cervical flexion, extension and rotation ROM immediately after DN and passive stretching to the levator scapula and UT bilaterally, with greater improvements at follow-up after 1 week.

There were no between-group differences at 24-hour follow-up in this dissertation study. It is possible that a 24-hour follow-up is insufficient to observe the full effects of DN. Koppenhaver et al[190] found a greater change in internal rotation ROM 3 to 4 days post-treatment

in subjects with subacromial pain syndrome after DN to the infraspinatus. In their study, the initial changes were small and statistically insignificant, but a longer duration of follow-up showed changes that were larger and statistically significant.[190] Campa-Moran et al[188] made a similar observation in their study that included DN in their methodology to compare ROM, PPT, and clinical outcomes after various forms of manual therapy. Improvements in ROM were greatest 1 week after the final DN treatment in all directions of cervical ROM except extension. The muscles that were treated did not limit extension, which may explain why extension did not improve as much as other directions.

There are concerns about the methodology in some of the studies that found increased flexibility immediately after DN. Some studies did not include a control or placebo group, therefore expectation of improvement may have influenced the subjects' performances on post-treatment testing.[5,186,188,189,192] The lack of a control group would not allow the researchers to account for the natural changes occurring in a condition over time. Some studies included subjects that were healthy and pain-free[186,189] or elite athletes,[191] which would limit generalizability to a typical clinical population. One study included only women ages 18-30 years with latent MTrPs, and while they did find a significant improvement in ROM after DN, the generalizability of the results to other patient populations is limited.[192]

Treatment dosage may play a key role in the effects of DN on flexibility, however research on the optimal dosage by condition does not exist at this time. One must be cautious to provide a stimulus that is therapeutic but does not result in excessive post-treatment soreness. In this dissertation study, subjects received DN to the multifidi of 2 spine segments bilaterally, and local twitch responses (LTRs) were not monitored. Other studies finding significant changes in ROM used a variety of durations per area treated, some as high as 1 to 2 minutes per

MTrP.[5,163,180,186,188] Campa-Moran et al[188] treated each MTrP for 2 minutes in the UT and levator scapula bilaterally. Haser et al[191] had subjects treated once per week, with each DN session lasting approximately 20 minutes. A significant improvement in ROM has been observed with a lower treatment volume, however these improvements were not observed immediately post-treatment.[190]

Remote Flexibility. When compared with literature on how DN affects local flexibility,[27,93,163,186-189,191] little research has been done on the remote effects on flexibility.[30,144,182,193] The immediate impact on remote flexibility that was expected did not occur. This contradicts the findings of studies that focused on endplate noise in muscles remote to the area of DN. A decrease in endplate noise may translate to an improvement in the ability of a muscle to lengthen. Hsieh et al[144] found a reduction in endplate noise in the biceps femoris after DN to the gastrocnemius in anaesthetized rabbits, but no reduction in endplate noise after sham DN. Two studies by Chou and colleagues found a decrease in endplate noise in MTrPs in the UT after DN to the distal UE, but not after sham DN.[30,182] It is possible that a rapid, transient change occurred but was not detected by the methodology for this dissertation study, given that remote flexibility was not tested until 10 to 15 minutes after DN.

Human and animal models show mixed results regarding SNS activation and muscle spindle sensitivity.[41-49] Animal studies[42,44,45] support suppression of the muscle spindle with SNS activation, however human studies[44,46,48] tend to demonstrate no change or an increase in sensitivity of the muscle spindle. EDA confirmed SNS activation to be greater in the DN group, but the remote muscle length post-treatment and at 24-hour follow-up did not differ between groups. A study by Grassi et al[43] showed suppression of muscle spindle afferents after activation of sympathetic nerves in animals, however they returned to baseline in 1 to 3 minutes. It is

possible that during the 5-minute post-treatment recording of physiologic data that the muscle spindle afferent suppression returned to baseline and therefore no difference was detected during flexibility testing. The treatment dosage may not have sufficiently activated the SNS to affect muscle spindle sensitivity, and this may have played a role in the lack of significant findings. Significant changes in remote flexibility and endplate noise have been observed in other human[30,182] and animal[144] studies using a higher treatment volume than was used in this dissertation study.

In this dissertation study, mean change scores were greater in the DN group for all remote flexibility measures except knee extension (KE) and straight leg raise (SLR) at R_2 immediately and 24-hours post-treatment, respectively. The change was not statistically significant (p>.05), nor did it surpass the MDC for inclinometry. Previous research has shown the MDC for digital inclinometry to be 9°.[126] Another reliability study on hamstring flexibility tests have found passive SLR testing and active KE testing to have an MDC of 6-8°.[127] Both studies that determined values for MDC were performed on healthy subjects and therefore might not be the best estimate of the MDC for flexibility tests in individuals with chronic low back pain (LBP).[126,127] Further examination of change scores for remote flexibility showed that none of the 95% CI included the MDC for digital inclinometry or hamstring length testing. Until MDCs and MCIDs are established for the hamstrings in a clinical population, the increase in remote flexibility of the DN group cannot be considered a meaningful change.

KE is mainly limited by hamstring length, but SLR can be limited by other structures.[194,195] This may explain in part why SLR was unchanged after DN. The ankle remained in a resting position to minimize the effects of neurodynamics on the SLR data,[196] but research shows that even with the ankle plantarflexed there can be increased activity in the rectus femoris,

gluteus maximus, gastrocnemius, soleus, biceps femoris and tibialis anterior that can limit ROM.[195] Even small amounts of involuntary muscle activity can reduce passive hip flexion during the SLR test.[197] The research assistant expressed that some subjects had difficulty relaxing their leg during passive testing, despite consistent verbal cues and repositioning by the assistant. The inability of the subject to relax and allow for passive movement until R_1 and R_2 were reached may have introduced some error into the data.

Segmental Effects of Dry Needling

As stated previously, pain modulation after manual therapy acts on peripheral, spinal and supraspinal pathways.[72] The segmental effect of DN to the TL junction that was expected was not observed in this dissertation study. These results conflict with others studies that have found significant segmental effects in hypoalgesia after DN.[50,92] In one study subjects had DN to the supraspinatus, followed by PPT testing to the infraspinatus and gluteus medius.[50] The authors found an increase in infraspinatus PPT after DN to the supraspinatus, but no difference in gluteal PPT. Supraspinatus and infraspinatus are segmentally linked by C5, but share no segmental connections with gluteus medius. Baeumler and colleagues[92] also found an increase in PPT in an area that was segmentally linked to the needling site but no change extra-segmentally. Significant differences in PPT of the extensor carpi radialis brevis were found immediately[93,163] and one week[93] after DN to the infraspinatus, which have a common motor innervation at C6. The hamstrings and TL multifidi do not share a common motor innervation, and the previously mentioned studies included muscles with a common contribution for motor innervation.[50,92,93,163] This could explain why the results of this dissertation study conflicted with the studies that concluded DN had segmental effects on hypoalgesia.

To better understand what occurred in this dissertation study, mean change scores in PPT were examined for the DN group beyond the presence of statistical significance. Mean change scores were positive when compared with baseline, indicating decreased sensitivity, in all areas across all times for the DN group. It is plausible that DN to the TL junction had an extra-segmental effect of hypoalgesia, which would explain the positive change scores in UE and lack of significance between the UE and LE. Substance P is a neuropeptide that is involved in the transmission of pain peripherally and through the central nervous system, and extra-segmental changes in substance P have been observed in the spinal cord of rabbits in the cervical and thoracic regions after DN to a muscle innervated by the lumbar spine.[144] These findings may help explain the extra-segmental pain modulation that may have occurred in this dissertation study. The positive change scores in the UE and LE in this dissertation study, and the lack of a significant difference between the two, could imply an extra-segmental effect mediated by spinal or supraspinal antinociceptive processes.

Extra-segmental hypoalgesia has been seen in human DN studies.[29,77,193,198] Salom-Moreno et al[77] found between-group differences in changes in PPT locally and remotely after DN when compared with a no-treatment control group. Subjects had one treatment of DN to their affected lower leg and PPT increased bilaterally in the anterior tibialis, the second metacarpal, and the deltoid. Mejuto-Vazquez et al[29] also found a significant widespread increase in PPT immediately after treatment and at 1-week follow-up when compared with subjects who had no treatment. In their study, the UT was treated with DN, and differences were found locally and extra-segmentally at the anterior tibialis and second metacarpal. These changes were observed bilaterally. Kamali et al[198] randomized 40 participants to receive DN to the UT or infraspinatus, and looked at changes in PPT in the UT. They found significant within-group differences in PPT

of the UT after DN to the infraspinatus only, and concluded that hypoalgesia can occur remotely with DN. This implies that remote DN could be effective for reducing pain and disability in patients who are unable to receive DN to their primary area of pain because of hypersensitivity, fear, or skin lesions. However, one should consider that the UT group may have been experiencing post-treatment soreness and this could account for the lack of within-group significance in the subjects who had DN to the UT.

Pain is a complex sensation and is dependent upon a balance of excitatory and inhibitory neurons.[153] The periaqueductal gray (PAG) is responsible for integrating the ascending and descending information, and its connection to the rostral ventral medulla (RVM) is tasked with engaging the endogenous opioid and cannabinoid systems, as well as other neurotransmitters that modulate the overall pain experience.[153] Manual therapy is thought to stimulate the PAG, resulting in immediate hypoalgesia.[74] Descending pathways from the PAG and RVM to the spinal cord use noradrenaline and serotonin to further inhibit the pain message.[153]

Increased EDA was observed in the DN group immediately post-treatment. EDA is a purely sympathetically-mediated physiologic response, and this confirms some level of sympatho-excitation from DN. The SNS can modulate pain in two ways. First, SNS activation leads to stimulation of noradrenergic and serotonergic cells in the brainstem, which modulate messaging in the dorsal horn of the spinal cord. Second, SNS activation leads to the release of endogenous opiates, which bind to receptors on the afferent neurons, projection neurons within the spinal cord, cortical neurons, and cells within the brainstem.[33] Both pathways result in suppression of nociception, which ultimately results in hypoalgesia or analgesia. Subjects with chronic musculoskeletal pain, as were the subjects in this dissertation study, have impaired pain modulation. Having suppressed pain inhibition pathways may lead to a decrease in the analgesic

effect of DN. This phenomenon has been observed in an acupuncture study on subjects with chronic neck pain.[152] Humans can be more or less responsive to SNS activation based on the duration and course of their condition,[199] and individuals with chronic LBP have lower dopamine levels, lower dopamine release with experimental pain, and a diminished ability to activate their endogenous opioid system.[200,201] This may explain why change scores indicated decreased sensitivity with PPT, but changes were small and below the MCID for PPT.[145,202]

The diminished inhibition of pain resulting from dysfunction of these pathways could have also caused subjects in this dissertation study to be more susceptible to the effects of temporal summation with repeated PPT testing.[152] In this dissertation study, the PPT testing occurred in the same order for each subject, with the lateral hamstrings tested last. PPT values gradually declined in many subjects within a session of data collection, however this was not quantified as part of the analysis. Anderson et al[203] observed temporal summation in up to 72% of subjects when tested with repetitive heat stimulation, however cluster analysis labeled only 29% of subjects into a group that experienced a significant temporal summation. It is worth noting that the subjects in the aforementioned study had a mean age of 22.9 years (SD = 3.2) and had no clinical pain at the time of testing.[203] This dissertation study had an older sample and subjects were seeking physical therapy for their symptoms, indicating a recent bout of clinical pain. If temporal summation did occur, it could have lowered the medial hamstrings and lateral hamstrings PPT values, which would skewed the data toward showing no segmental effect from the sympathetic connection between the TL junction and the LEs.

The increase in PPT observed in this dissertation study may have been a result of habituation, which is a learned response to repeated stimulation. This has been seen in a test-retest and reliability study which did not involve an intervention.[204] The authors stated that

habituation can occur from diffuse noxious inhibitory control and the release of endogenous opioids during the testing. It is plausible that the small and insignificant change in PPT was a result of habituation rather than a direct cause of the DN itself.

Another possible explanation for lack of significance of PPT measurements is a subject's emotional state during testing. Anxiety and other emotions have been found to influence pain responses in humans, specifically with chronic pain.[33,205] Beyond needle anxiety, no other emotion was quantified in this dissertation study so its influence on the perceived pain level during PPT testing cannot be evaluated. Subjects were also advised to avoid exercise, caffeine, alcohol and analgesics prior to testing, however compliance with these guidelines was not monitored.

Finally, it is plausible that the treatment dosage in this dissertation study was not high enough to see the extra-segmental changes observed in other studies. Extra-segmental differences were observed after 30 seconds[29,77] to up to 2 minutes[193] of DN to MTrPs, and the number of MTrPs and the total duration of treatment were unspecified. Kamali et al included 3 session of DN to the most irritable MTrP, which was treated until LTRs were exhausted. The authors did not specify the total time of each treatment.[198] Subjects had a total of 1 minute of DN in this dissertation study, and this may have been an insufficient stimulus for hypoalgesia to occur.

Heart Rate Variability and Clinical Outcomes after Dry Needling

The results of this dissertation study did not support the hypothesis that the immediate post-treatment LF:HF ratio of HRV would correlate with clinically meaningful outcomes, such as the numeric pain rating scale (NPRS), global rating of change (GRC), and Oswestry Disability

Index (ODI) scores. The lack of correlation between HRV and clinical outcomes and the probable contributing factors are discussed in this section.

Numeric Pain Rating Scale. In this dissertation study, NPRS scores at 24-hour follow-up were not correlated with LF:HF ratio values. The most likely explanation for this observation is that subjective pain ratings in the DN group may have been influenced by post-treatment soreness at 24-hour follow-up. In one study greater than 90% of subjects reported some level of post-treatment soreness after DN, and the amount of soreness was directly related to the number of LTRs elicited during DN.[206] This soreness dissipated completely after 72 hours,[206] however this dissertation study did not include a follow-up beyond the duration that post-treatment soreness would have dissipated. Campa-Moran et al[188] also showed no improvement in pain ratings immediately after DN treatment, but changes were significant at 1-week follow-up. The follow-up duration may have been insufficient to show the full benefit of pain relief after DN.

LTRs were not quantified in this dissertation study, so it is not possible to infer the magnitude of soreness the DN group may have experienced based on LTRs. The significance of LTRs has been subject to some disagreement in the DN research.[9,35] Microdialysis to muscles with active, latent, and no MTrPs showed a decrease in pro-nociceptive biochemicals, such as substance P and CGRP, after an LTR.[207] While it was not the purpose of the microdialysis study to quantify pain relief, the theoretical models on which the study was developed would suggest that this would result in decreased pain. However, Koppenhaver et al[35] found no between-group differences in pain when subjects were dichotomized into groups of those who experienced LTRs and those who did not. Thus, monitoring LTRs may not have provided any additional insight into understanding the NPRS scores in this dissertation study.

While the mean change in NPRS scores for the DN group was slightly greater, it was below the MDC of 2 points.[134] This suggests that any observed change may be measurement error. Subjects were only asked about their current level of LBP at the time they arrived on Day 2. In retrospect, a broader representation of a subject's current pain level should have been obtained. An example of this was used by Cleland et al[208] when the researchers took the mean of 3 pain ratings (current, worst and best level of pain) to denote a subject's pain rating. Alternatively, having subjects rate their highest pain level over the past 24-hours or pain level when the subject engaged in pain-provoking activities would have been a better indicator of improvement.

Low treatment dosage may have been a factor in why there was minimal change in the NPRS scores and no correlation with HRV in this dissertation study. Improvements in pain rating have been observed in studies using higher treatment dosages.[5,22,182,187,188] Ceballos-Laita et al[187] found a significant improvement in subjective pain ratings after DN when compared with sham DN, however their study involved 3 DN treatments compared to only 1 in this dissertation study. Campa-Moran et al[188] treated each MTrP for 2 minutes and subjects had 2 treatments separated by 48 hours. The subjects had a significant decrease in pain rating at 1 week after the final treatment, but pain ratings were not significantly improved from baseline immediately after each treatment.

In this dissertation study, both groups experienced a reduction in NPRS scores on Day 2. Changes in pain after manual therapy intervention can result from neurophysiological responses relating to the setting where the treatment took place, the patient-provider relationship, beliefs, expectations, and any other external cues the environment provides.[72,209] These are often referred to as contextual factors.[72,209,210] Positive contextual factors activate opioid, endocannabinoid, and

dopaminergic systems.[210] One cannot discount the presence of positive contextual factors acting on pain pathways in this dissertation study. Such examples of this are the clinical experience and reputation of the primary investigator, a quiet environment for data collection, and the study occurring in a familiar place for many of the subjects.

A response to sham DN has been observed in the dorsolateral prefrontal cortex, rostral anterior cingulate cortex, and midbrain, which are responsible for pain recognition. When the dorsolateral prefrontal cortex is triggered, it is possible that the endogenous opioid system can be activated.[211] Activation of these areas in the brain can induce a phenomenon of "placebo analgesia."[209,212] Additionally, placebo analgesia can be diminished by administration of the opioid antagonist drug naloxone, which blocks the response of several brain structures, including but not limited to the PAG and RVM. The placebo condition is no longer viewed as fully inert because it acts on brain areas similar to those involved in pain modulation of active treatments.[149] Sham treatments have a small, yet possibly significant, effect on perceived pain. This was observed in this dissertation study given that both groups experienced a reduction in NPRS scores at 24-hour follow-up. Including a control group would have allowed for interpretation of the magnitude of the placebo effect in this dissertation study. If both DN and placebo had outperformed a no-treatment control group, the treatment did not fail because it was still superior to the natural progression of the condition.[149]

The issues with using LF:HF ratio of HRV as the indicator of SNS outflow for this hypothesis were mentioned earlier in this chapter. A better metric for measuring SNS outflow would have been EDA since it has no contribution from the PNS. Analysis of the correlation using post-treatment EDA showed no significant correlation for pain at 24-hour follow-up (p=.09). Manual therapy induced hypoalgesia with SNS activation is thought to be more

effective in a clinical population with a higher level of pain than the subjects in this dissertation study,[74] and this is a possible explanation as to why the correlation was not significant.

Global Rating of Change. GRC scores did not correlate with LF:HF ratio of HRV. Further analysis of the GRC scores showed they were greater for the DN group, however the difference was not significant (p=.23). As mentioned previously, LF:HF ratio of HRV may not be the best indicator of sympathetic outflow; EDA is a superior metric of sympathetic outflow because eccrine glands have no PNS innervation. However, the analysis was repeated with post-treatment EDA and the correlation was not significant (p=.51). It should also be noted that 64.8% of subjects correctly identified their group allocation, despite the sham needle being shown as indistinguishable from DN in individuals who have never had DN.[140] Subjects were primarily recruited from a clinic with 4 physical therapists certified in DN, so it is possible that subjects saw how patients responded to a DN treatment and subsequently based their perception of their group allocation on if they responded in a similar fashion. Subjects who correctly identified the sham procedure may have rated their GRC as lower if they assumed the sham treatment would not influence their symptoms.

GRC has been criticized for its susceptibility to recall bias, however shorter follow-up durations are less susceptible to poor recall.[130,213] Recall bias was likely not a factor in the low GRC scores given that subjects were asked to recall functional status from the previous day. It is possible that a 24-hour follow-up is insufficient to appreciate a true functional change, and this has been observed before in a study on manual therapy to the thoracic spine.[208] Data collection in this dissertation study occurred on a consecutive Saturday and Sunday. Most subjects did not have an opportunity to work or travel, and therefore could not have observed functional changes associated with those two activities. Post-treatment soreness and the limited ability to engage in

tasks that would provoke pain may have influenced GRC scores, and therefore a longer follow-up duration may be more representative of true change.

Oswestry Disability Index. There was no correlation between ODI scores at follow-up and LF:HF ratio of HRV. The lack of correlation could be a result of several factors. First, the ODI may not have been the best assessment of physical function for this dissertation study. Because data collection occurred on a consecutive Saturday and Sunday, most subjects did not have the opportunity to commute to work (travel) or perform their usual job-related tasks. This means that subjects were not able to assess change in 20% of items in the questionnaire. Other DN studies have included a physical function test that could immediately quantify changes after treatment, unlike the ODI, which requires the subject to engage in all 10 constructs in order to quantify improvement.[27,189,214] The functional changes that would be captured by the ODI may be more appropriate for a study with a longer duration for follow-up.

Second, a majority of the subjects were already attending physical therapy, with some of them approaching discharge. As a result, their ODI scores were low. Research has shown that a 6 to 9% decrease in ODI score indicates meaningful improvement.[53,215,216] Using an MCID of 9%, only 4 subjects experienced a clinically meaningful improvement. Further examination of the ODI data showed a mean improvement of 3.6% (95% CI 2.0, 5.2) in the DN group and 1.9% (95% CI 0.4, 3.3) in the sham group. The group differences were not significant (p=.10). This dissertation study only looked at changes in 24 hours, and the studies that established the psychometric properties of the ODI had longer follow-up durations.[215,216] A study by Dawson et al found mean scores of 9.7% in subjects with "serious back pain" but who were not seeking treatment for their LBP.[217] Their calculated MDC of 6.4% is still greater than the mean change

scores and upper bounds of 95% CI for both groups in this dissertation study, thus change in ODI scores are likely not clinically meaningful, or are a result of measurement error.

Third, the LF:HF ratio of HRV is an imperfect measure of SNS activity because of the mixed input from the two branches of the ANS, as well as other unidentified factors. Using this metric as an indicator of sympatho-vagal balance assumes a linear relationship between the SNS and PNS that does not exist.[170] As stated previously, EDA would have been a superior metric to LF:HF ratio because it is exclusively mediated by the SNS.[62,97]

The clinical outcomes results in this dissertation study may be attributed to sham needling procedures not being completely inert. Sham needling can result in a release of endorphins or an expected positive outcome,[218] which may have elevated GRC, ODI and NPRS responses in the sham group. Future studies should include a control group to more adequately assess the influence of a sham procedure on both physiological and clinical outcomes.

IMPLICATIONS OF THE FINDINGS

Implications for Practice

DN is one of many forms of manual therapy provided by PTs, and there continues to be little agreement on the mechanism of action. This dissertation study adds to the body of research on what aspects of a patient's condition DN can help, as well as possible mechanisms of action for DN. SNS activation leads to suppression of pain by acting on ascending and descending pathways within the spinal cord, as well as a release of norepinephrine which is a known antinociceptive neurotransmitter.[33,219] It has been hypothesized that restoring ANS balance can aid in treatment of chronic musculoskeletal pain, and there is evidence that effective treatments for musculoskeletal pain act on the ANS.[220] In order to appropriately assign treatments to patients, one must understand the mechanism of action for the treatment. EDA data confirmed a

significant increase in SNS activation immediately after DN, but these effects were not sustained. The transient nature of the SNS activation suggests there is little carry-over in the clinical effect DN may have on a patient's condition.

The results of this dissertation study support the results of other studies, which show an immediate local improvement in flexibility after DN.[5,27,30,180,186-188,190] Clinically, a physical therapist may want to prescribe exercises to strengthen muscles in the newly obtained range of motion in the same session as the DN. Previously painful activities should be reassessed after DN. A patient may be able to tolerate activities that were previously painful, or perform the same activities with a lower level of pain. Patient education should focus on movement patterns they were unable to perform prior to the DN, if applicable. The effects of DN were not sustained at 24-hour follow-up, which could mean that a patient needs additional DN treatments to receive the full benefit of increasing flexibility.

The remote benefits of DN remain less clear. To date, there is a greater body of research supporting the remote effects of mobilization and manipulation on pain and mechanical sensitivity.[51,76] This means that for LE symptoms, manipulation may be preferred over DN. This dissertation study may not have included a treatment volume high enough to elicit changes in the length of muscles remote to the area of treatment. This should not be interpreted as a failure of DN to created positive changes in flexibility in body regions remote to the area treated, but more evidence supporting the remote benefits should be obtained to justify choosing DN over other forms of manual therapy.

The data support that a single DN treatment is unlikely to have a profound long-term effect on flexibility, given that local changes in flexibility were no longer significant at 24-hour follow-up. Other reports have confirmed that DN to more than one muscle in a session, more

than one MTrP in a muscle, or to the same muscle across multiple sessions have resulted in significant changes in pain, ROM and function.[5,22,27,30,182,187,188,190] The lack of significant findings may have resulted from insufficient treatment volume, and this should be considered when using DN in a clinical setting.

Patients who have not had previous DN may be fearful of DN in certain high-risk areas, specifically the trunk because of the risk of pneumothorax. The mean change scores for PPT in the DN group were positive in locations remote to the treatment site. This suggests that patients may receive the benefit of hypoalgesia from DN to an area that is not their primary complaint of pain. While the mechanism behind why this change occurs is not fully understood, it can still provide benefit to a patient during a physical therapy treatment.

According to the model by Bialosky et al,[72] one cannot isolate the effects of the mechanical force on the tissue and assume it was the only cause of the improvement or decline in symptoms. Also, the neurophysiological data obtained in a manual therapy study is only meaningful if it is linked to patient self-reported outcomes. In this dissertation study, sympathetic activity was not linked to clinically meaningful outcomes, such as the ODI, NPRS and GRC. One reason for this lack of significance could be the positive contextual factors of the therapeutic encounter that were discussed earlier in this chapter. PTs should be mindful of contextual factors during their therapeutic encounters and adjust them to promote positive outcomes after manual therapy.

The following summarizes the clinical implications of this dissertation study:

1. DN activates the SNS, which may lead to a decrease in pain. The effects are not sustained at 24-hour follow-up, meaning multiple treatments may be required.

2. DN can increase the flexibility of the muscle that was treated. For remote flexibility improvements, there is more evidence for the efficacy of joint mobilization or manipulation.
3. Corrective exercises to increase strength in newly-obtained ROM should be issued the same day as the DN, given that the increase in flexibility was not sustained.
4. Physical therapists should consider DN to a remote location if a patient is fearful of DN to the area of primary pain.
5. Consider contextual factors as something to positively impact treatment outcomes.

Implications for future research

The metrics of the DVs chosen for SNS outflow in this dissertation study were adequate, however different aspects of the same DVs could be considered for future research. An example of this would be choosing phasic measures of EDA instead of or in addition to tonic EDA. Both have their methodological challenges, but phasic measures have been used more frequently in DN research.[22,23] Another example is choosing maximum ST rather than mean ST in each 5-minute recording block. Like other ANS measures, peripheral vasoconstriction after SNS activation is transient, and using maximum temperature would give a better impression of maximum vasoconstriction achieved after SNS activation.[162]

A future study investigating the effect of DN on HRV may use ECG instead of PPG because it is less sensitive to a subject's movement during data collection. This may also allow for data collection during the DN procedure. Subjects move their limbs when experiencing a LTR and this causes some artifact in the PPG wave. In this dissertation study, visual inspection of the wave and inter-beat intervals could compensate for most of the disruption of the wave if a subject moved his or her limb during recording, and this recommendation should not be

construed as PPG being inadequate to measure HRV. The waves with artifact cannot and should not be omitted because such omission would skew the results toward longer inter-beat intervals and higher HRV.[171] PPG waves do not rise to a sharp peak like ECG waves and therefore the exact location of the peak can be more difficult to derive. PPG data can also be affected by vascular tone and stroke volume, which may introduce additional error.[171] If PPG is used in future studies, one may consider Raynaud's phenomenon as an exclusion criterion since it can affect digital pulse readings. The sphygmic wave can have a lower amplitude,[221] which would introduce some error in determining the QRS peak on the wave, whether it be determined by computer software or manually. The subject that had an indiscernible PPG wave indicated a diagnosis of Raynaud's phenomenon on the intake form.

The only DV in the hypothesis relating to the segmental effects of DN was PPT, and the areas chosen for PPT were not myotomally connected to the muscles or spine segments treated. Previous studies on the segmental effects of manual therapy that used PPT as an outcome variable tested areas that were myotomally connected to the muscle being treated.[50,92,93,144,163] For this dissertation study, those muscles would have been the psoas major, quadratus lumborum, and internal obliques. Future research should investigate changes in PPT in an area that is segmentally linked by myotome to the area being treated. The segmental effects of DN could be further investigated using EDA readings in the LE and UE to determine if SNS outflow is limited to the extremity that is segmentally-linked to the area treated or if the effect is global.

Research in the remote effects of DN has taken a "distal to proximal" approach in human and animal models,[10,30,144,182] and this dissertation study is among the first to take a "proximal to distal" approach in its methodology. The results of this dissertation study did not agree with others investigating the remote effects of DN, but this should not be viewed as a failure of DN to

have remote effects in a "proximal to distal" manner in light of some of the methodological concerns discussed in this chapter. Future research should be done to confirm or refute the findings of this dissertation study in order to further understand the mechanisms of DN.

According to the results of this dissertation study, one treatment of DN is sufficient to create local change in ROM. There is evidence that multiple DN treatments over time to the same muscle can create greater flexibility outcomes locally[187] and remotely.[144] There is also evidence that the benefits of DN may not be seen until 3 to 4 days post-treatment.[190] A future study that analyzes ROM changes after multiple DN treatments at a fixed interval, as well as longer follow-up, should be considered. Such a study would also provide an idea of how many treatments are required for maximum efficacy and after how long a patient is likely to see positive benefits. Additionally, there is little agreement on the optimal dosage for DN, and therefore it is plausible that the 2 spine segments treated bilaterally for 15 seconds each was not enough to create the profound changes that were observed previously with higher dosage.[144,187,188,191,206] Including multiple DN treatments over time or DN to multiple MTrP or muscles in one session may have led to significant findings in the clinical outcomes and remote flexibility in this dissertation study. Future research should focus on varying the dosage of DN to determine if increasing treatment volume effects pain modulation, flexibility and functional outcomes.

A methodological shortcoming of this dissertation study is that active MTrP were not confirmed at the TL junction, nor were LTRs monitored. The spinal levels that were treated were also predetermined. Predetermining the spine segments helps with standardizing the treatment protocol in a study, but it is not representative of how patients are treated in the clinic. Subjects may have had other active or latent MTrP that contributed to their symptoms, and a better

clinical outcome may have occurred with treatment directed to those areas. Subjects may have experienced more profound changes if DN had been directed at the most active MTrP. This phenomenon was observed in an animal model in which superior outcomes were seen when DN was directed toward a known MTrP.[184] Additionally, subjects were not excluded from this dissertation study if they did not have MTrP in the T12 or L1 multifidi, or if active MTrPs were present unilaterally. Locating MTrP prior to DN is more representative of how the treatment is delivered in the clinic, and therefore should be included in future studies of clinical outcomes in DN research. It is worth noting, however, that studies have shown mixed results in one's ability to accurately palpate and diagnose a MTrP, varying from poor[222,223] to moderate.[224,225]

Dry needling is rarely, if ever, the only treatment modality used in a patient's plan of care. It should not be used in isolation despite the positive changes in local flexibility and changes in aspects of SNS activity, but rather as a part of a comprehensive and individualized treatment program determined after examination. More recently, studies have included DN as a part of a multimodal treatment program to determine if DN resulted in better outcomes, however the results are mixed.[226-230] This dissertation study did not include other forms of manual therapy for comparison. Campa-Moran et al[188] found significant within-group changes in ROM for the DN group, but the changes were not superior to two other forms of manual therapy. Other forms of manual therapy should also be included in future studies to confirm these findings.

A 24-hour follow-up was used in this dissertation study to assess short-term changes in ROM, flexibility, PPT, pain, disability, and measures of SNS outflow. This may have been insufficient to observe improvements in pain and disability given that most patients and subjects feel some level of post-treatment soreness after DN.[206] Post-treatment soreness may skew NPRS and ODI ratings if follow-up is less than 72 hours, which is when post-treatment soreness

dissipates. Additionally, some of the benefits of DN may not be seen until 3 or more days after DN.[188,190] Future studies should include data collection immediately after DN, as well as a longer follow-up duration.

The H reflex may be superior indicator of the remote effects of DN on muscles instead of the flexibility tests used in this dissertation study. Flexibility testing is an indirect measure of alpha motoneuron excitability and muscle spindle sensitivity. Electromyography may have been a better method of quantifying changes in muscles remote to the site of DN because it is capable of recognizing the effect in a much shorter time frame. In this dissertation study subjects remained connected to the sensors for greater than 5 minutes after treatment. It is plausible that the an attenuation of the H reflex occurred but was not detected in the flexibility testing that took place 10 to 15 minutes after the DN was completed. A future study should include the H reflex as a DV to determine if there are rapid and transient changes in muscles distant from the treatment site, and the clinical implications of these changes should be considered.

Finally, minimum requirements for the ODI and NPRS were not set when designing this dissertation study. The scores on these tests were lower than those typically seen upon initial evaluation of patients seeking physical therapy for their LBP. This prevented the researchers in this dissertation study from capturing the benefits of DN in patients with higher disability from their higher pain levels. Future study designs should include minimum scores in order to adequately reflect the benefits of DN in an average clinical setting.

LIMITATIONS AND DELIMITATIONS

While many steps were taken to try to minimize bias, there were still some limitations associated with this dissertation study. First, there is no true placebo for DN, therefore a placebo-controlled, double-blind DN study is technically impossible in awake and alert subjects.[36] A

study by Mayoral et al[38] used novel blinding methodology for their placebo. Subjects were undergoing total knee arthroplasty and were randomly assigned to either a DN group or placebo group. Because the subjects were under anesthesia, they were unable to identify which treatment they had received. This has been the most effective blinding scenario to date, but it is not appropriate for most DN studies.

For many years, researchers have tried to develop a more effective placebo, but have found that any stimulation on the skin influences the limbic system and has a neurophysiological effect.[231] Because the limbic system influences the ANS, a non-penetrating "sham" treatment would still have an effect on HRV, ST, and other measures of SNS activity.[36] This was observed in the post-treatment recordings of the sham DN in this dissertation study in some of the variables monitored. Quantifying the amount of the ANS activity during DN or sham DN was not an objective of this study and therefore was not included as part of the data analysis. Quantifying the ANS activity during the treatment condition may have given additional information on the neurophysiological effects of both scenarios.

Many attempts were made to ensure adequate blinding in this dissertation study. Bang et al[232] created a novel "blinding index" to calculate a value that would determine if blinding was effective in a clinical trial. Blinding is consider effective when the coefficients calculated for each group are of similar magnitude, but one is positive and one is negative, and the 95% CIs include 0.[233] In this dissertation study, the blinding index was -0.56 (95% CI -0.67, -0.45) for the DN group and 0.52 (95% CI 0.31, 0.73) for the sham group. The indices were similar in value, with one positive and one negative, however neither confidence interval included 0, which means blinding was ineffective. It should be noted that the formula from Bang et al[232] places greater value on decisive responses and de-emphasizes "unsure" responses, which may have

artificially inflated the index given that nearly 41% of respondents in the sham group and 30% in the DN group selected "unsure." Bang et al[232] stated that the index should be used with caution when the "unsure" respondents total more than 30%. The failure of adequate blinding in this dissertation study may be attributed to DN being a common treatment in Maryland. Subjects may have had indirect exposure to the technique, meaning they have either seen it done by a physical therapist in the clinic when they were attending their physical therapy, or they had discussed it with a friend or family member who had DN. Subjects were advised on Day 1 of the protocol not to discuss their experience with someone who had DN until group allocation was revealed on Day 2. This was done to try to decrease outside influence on the subject's perception, but this would not have affected discussions prior to participation on Day 1 or what they observed in the clinic.

Repeated flexibility measures on subjects introduced testing effects, which refers to the effect pre-testing and repeated testing would have on the DV.[234] Repeated passive excursion of the limb may have increased flexibility as the testing progressed, regardless of group allocation. The research assistant used the same cues for all subjects to help mitigate this. The order of the tests should have been randomized to negate the effects of repeated testing on the outcomes of flexibility testing.

Experimental bias was managed by blinding both the primary investigator to the results of testing on both days and by blinding the research assistant to group allocation. Therefore, the primary investigator and research assistant could not influence the post-treatment and follow-up measures based on their expectations of what should have occurred. Blinding was less effective than expected for reasons discussed previously, and a subject's expectation of his or her treatment response may have influenced their performance on post-treatment testing.

This study only represents the response to DN in individuals with lower disability and pain ratings. The subjects' NPRS and ODI scores at the initial visit were low when compared to a typical clinical population. Tonosu and colleagues[235] calculated normative data using ODI scores in 100 males and females across 6 decades of life, and they estimate a mean ODI score of 7.2% in the 4th decade of life, which encompasses the mean age of participants in both groups. In their study, the average across all ages was 8.7%.[235] The cut-off point for subjects with disability from LBP was estimated to be 12.0%. In this dissertation study the mean scores for both groups were 12.3% (SD=7.0) on Day 1 and 9.6% (SD=7.7) on Day 2. Additionally, mean NPRS scores were low; mean scores were 2.6 (SD=1.4) on Day 1 and 1.8 (SD=1.5) on Day 2. Subjects were only asked to rate their current level of pain when they arrived for study participation, which may not fully describe their pain pattern throughout the day. A subject's level of pain with activity or worst pain in the past 24 hours should have been obtained in order to more accurately describe the benefits of DN.

Subjects participated in this dissertation study at varying points in their course of PT, and this was reflected in the wide range of ODI scores (0-40% on Day 1 and 0-46% on Day 2) and NPRS scores (0-6 on Days 1 and 2). Two subjects did indicate 0% disability on their ODI despite having enough pain and disability to seek physical therapy treatment. A higher pain level probably urged them to access physical therapy, and it is assumed that the physical therapy interventions improved but had not yet resolved their initial complaints of LBP. Had subjects participated in the study earlier in their course of physical therapy there may have been a more profound effect from the DN.

In the interest of feasibility, data collection took place on a Saturday and Sunday in one weekend. The ODI was used to determine functional changes after DN, but it was likely not the

best indicator of functional change in a 24-hour period. It should be noted that nearly all subjects did not engage in normal work activities or travel after Day 1 participation, so any change in those items could not be assessed. This can be address in the future by using a longer follow-up duration or by using a physical test post-treatment, with which immediate changes would be more apparent.

Respiration can impact PNS activity[80] but was not recorded in this dissertation study. It is possible that the two groups varied in respiration rate, which could explain the lack of significance in the HRV data. Respiration rate should have been included as a covariate in the analysis to adjust for its effect on the PNS.[236] Needle anxiety was quantified on Day 1 of data collection, but other aspects of stress and anxiety were not quantified. Emotional and other forms of stress are known to affect ANS output, which would be reflected in EDA, ST and HRV measurements.[237] A reliable and valid questionnaire quantifying emotional stress could be used in future studies as a covariate to control for some of the variability in ANS measures.

The order of PPT testing was not randomized, and this may have resulted in temporal summation impacting the medial and lateral hamstring PPT measurements. Temporal summation is a C fiber-mediated phenomenon, and it occurs from increased excitability in the dorsal horn of the spinal cord where pain messaging can be modulated. The researchers in this dissertation study observed a progressive decrease in PPT within subjects, possibly resulting from temporal summation. It is more common in subjects with chronic pain. The stimulus used in most temporal summation protocols is 0.3 to 1.0 Hz, which is a higher frequency than was used in this dissertation study.[203] The possible effects of temporal summation should not be discounted, and it is not possible to determine if the frequency of PPT stimuli in this dissertation study impacted the results.

Delimitations of this study included inherent error in palpation, using volunteers, not controlling for contextual factors and the choice of needle manipulation technique. This dissertation study did not include a control group, which would have represented the natural progression of LBP over the course of 24 hours. The choice to not include a control group was one of feasibility. DN has been in the practice act since 1989 in Maryland, and therefore is a common treatment modality in physical therapy. Previous experience with DN was one of the more frequent disqualifiers for potential subjects, and this would have presented recruiting challenges for a larger sample size.

Using palpation to identify bony landmarks is known to have poor reliability, however reliability is improved if the clinician doing the palpation is experienced, the same clinician identifies all locations, multiple bony landmarks are used to confirm the location, and a standardized protocol is established.[117,135] In this dissertation study, the primary investigator had 15 years of clinical experience in orthopedic practice at the start of data collection. Error in palpation was further managed by having the primary investigator locate spine segments on all subjects using consistent palpation techniques discussed in the methodology chapter of this dissertation study, which was adapted from Snider et al.[117]

A sample of volunteers was likely not representative of a patient population, however this type of sample was chosen to improve feasibility of the study design. This dissertation study included both males and females. Females have differing pain sensitivities based on the phase of their menstrual cycle.[238] An increased sensitivity to pain may lead to an increase in SNS stimulation during DN, however in the study sample 65% of subjects were either male, menopausal, or had no menstrual cycle secondary to use of prescription contraceptives. Therefore, menstrual cycle was unlikely to be a meaningful covariate in this dissertation study.

Males and females also differ in HRV. Men have greater sympathetic tone and less parasympathetic modulation.[239] This could have explained in part the wider range of values in HRV data. The gender-related changes peak at age 35-44 and dissipate after age 55.[239] Random sampling and having both genders equally represented in each group helped to minimize the effect.

This dissertation study did not specify needle anxiety as an exclusion criterion. An estimated 22% of individuals experience some needle anxiety or phobia, with 8.2% being "unreasonably intense."[240] The level of anxiety a subject experienced was quantified using a visual analog scale, and scores were used as a covariate in the SNS analysis. Severe needle anxiety that is "unreasonably intense" was not encountered in this study because those with intense needle anxiety would not volunteer for a DN study.

There are many forms of needle manipulation used in DN, however this study only investigated a form of needle manipulation called "pistoning," which is akin to the "fast-in fast-out" popularized by Hong in order to treat as many MTrPs while minimizing tissue damage.[9] This technique is further described as manipulating the needle "up and down at a rapid frequency, with a rate of approximately 1-2 strokes per second without fully withdrawing the needle from the skin."[241] Although keeping the needle in situ for a predetermined duration would have been easier to standardize, it does not reflect the way patients are treated in the clinic.

Currently, the most common method used to analyze HRV is ECG.[60,242] PPG was chosen over ECG for several reasons. First, ECG would require 3 electrodes and leads to be placed prior to data collection. Because the subject was placed in prone, it was possible that movement of the skin while changing positions from sitting for electrode placement to prone for data collection would have caused the electrodes to be improperly positioned. Second, the ECG signal can be

contaminated by electrical signals from muscle activity. For these reasons as well as the strong correlation between PPG and ECG,[60,242] PPG was chosen for this dissertation study.

Contextual factors refer to all the circumstances that surround a clinical encounter for treatment, whether it be active treatment or sham treatment, and are difficult to quantify and standardize.[210] Memories, emotions, and the psychological state of the subject can influence treatment outcomes. Data collection took place in the clinic where most subjects were attending physical therapy. The lower ODI scores at baseline imply that subjects were experiencing positive benefits from physical therapy. The primary investigator was employed at the clinic so there was a level of familiarity for the subjects. These positive contextual factors could have activated neurotransmitters, such as endocannabinoids, dopamine and oxytocin.[210] This may have affected the DVs in the dissertation study, such as PPT, NPRS, GRC, and ODI. The positive contextual factors could have influenced the DVs enough in the sham group to result in the lack of significance between groups.

Segments treated with DN were predetermined, and the most symptomatic MTrPs for each subject were not identified and treated. While this improves the standardization and repeatability of this study, it does not represent how patients are treated in the clinic. The treatment dosage was predetermined as 15 seconds of pistoning in the multifidi at T12 and L1 bilaterally. This may have been a factor in the lack of significant findings in measures of SNS activity, flexibility, and clinical outcomes. While the dosage in this dissertation study was low, one must use caution to avoid excessive dosage resulting in a deterioration of a subject's or patient's condition. In an animal model, beta endorphin levels decreased and substance P levels increased after 5 consecutive days of DN, meaning there is the possibility that a higher treatment dose would increase pain in human subjects.

RECOMMENDATIONS

Recommendations for clinical implementation of the results include continuing to use DN for immediate improvements in local flexibility. Because DN was not compared to other forms of treatment in this dissertation study, one should not conclude it is superior to mobilization, manipulation, exercise or any combination of the aforementioned treatments. DN should not be used as the only modality, and should be implemented as part of a comprehensive and multimodal treatment program when trying to improve flexibility.

DN does affect the SNS, as indicated by significant differences in the only DV that was purely sympathetically-mediated. Other DVs selected to confirm these findings did not reach significance, and the reasons for this observation were discussed previously in this chapter. DN did not evoke a segmental response of hypoalgesia when directed to spine segments that are responsible for sympathetic outflow to the tested, however extra-segmental hypoalgesia should be considered as a possible effect of DN given that UE and LE PPT measures had positive change scores. DN to muscles outside the primary area of pain should be considered when patients are unable to receive DN to that area because of skin lesions, fear of adverse outcomes, or if the physical therapist is uncomfortable or unfamiliar with treating a particular area.

SUMMARY

This chapter presented the discussion of findings from the analyses that were established a priori for this dissertation study. In subjects with LBP, DN evoked a sympathetic response that presented as increased EDA; both ST and HRV did not change in accordance with EDA and this observation could be explained by the transient nature of ST changes and the parasympathetic contribution to the LF spectral power of HRV. DN can improve local, but not remote, flexibility in subject with chronic LBP. Hypoalgesia after DN may present extra-segmentally, but in a

chronic pain population one cannot discount the effects of temporal summation, which may have skewed PPT measurements in the LE toward greater sensitivity. There was no correlation between clinical outcomes and changes in LF:HF ratio of HRV immediately post-treatment. The LF:HF ratio of HRV may not have been the best indicator of SNS activation, and other metrics should be considered for future studies.

From a clinical perspective, physical therapists should consider DN as part of a multimodal treatment program to address functional limitations secondary to restricted ROM. Other aspects of this study did not result in significant findings, and the methodological concerns that likely attributed to the lack of significance were discussed. A common theme in the discussion of the hypotheses were low disability and pain ratings, insufficient treatment dosage, and failing to confirm the presence of active or latent MTrP at the segments that were treated. Future DN studies should address these limitations.

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Appendix 1

PARTICIPANT DATA FORM

Name:_____ Date:_____ Sex: __M __F
DOB:_____ Phone:_____
Height:_____ Weight:_____

Duration of current episode of low back pain: _____ days / weeks / months

Do you have or have you had any of the following:
__Autoimmune disease __Abnormal bleeding __Needle phobia
__Neurological disorder __Cognitive impairment __Infection
__Skin lesion __Low back surgery __Pneumothorax
__Diabetes __Other

If yes, please describe:_____
_____
_____

Are you taking any medications? __Y __N
__Antidepressant __Anti-anxiety __Pain reliever __Other
If yes, please describe:_____
_____

Have you ever had dry needling before? __Y __N
If yes, please describe:_____
_____
_____

Please rate your fear of needles:

0	1	2	3	4	5	6	7	8	9	10
none										extreme

Please rate your pain today, 0 = nothing and 10 = worst pain imaginable:

0	1	2	3	4	5	6	7	8	9	10
none										extreme

For females:
Are you currently pregnant? __Y __N
Date of first day of last menstrual period: _____

Appendix 2

Name_____ Date_____

Modified Oswestry Low Back Pain Questionnaire

This questionnaire is designed to enable us to understand how much your low back pain has affected your ability to manage your everyday activities. Please answer each section by marking the one number that most applies to you, **circle only one.** We realize that you may feel that more than one statement may relate to you, but please **just mark the one that most closely describes your problem.**

Section 1: Pain Intensity

0 The pain comes and goes and is very mild
1 The pain is mild and does not vary much
2 The pain comes and goes and is moderate
3 The pain is moderate and does not vary much
4 The pain comes and goes and is severe
5 The pain is severe and does not vary much

Section 2: Personal Care

0 I do not have to change my way of washing or dressing to avoid pain
1 I do not normally change my way of washing or dressing even though it causes me pain
2 Washing and dressing increases pain, but I manage not to change my way of doing it
3 Washing and dressing increases pain and I find it necessary to change my way of doing it.
4 Because of the pain I am unable to do some washing and dressing without help
5 Because of the pain I am unable to do any washing and dressing without help

Section 3: Lifting (skip if you have not attempted lifting since the onset of low back pain)

0 I can lift heavy weights without extra low back pain
1 I can lift heavy weights but it causes extra pain
2 Pain prevents me lifting heavy weights off the floor
3 Pain prevent me lifting heavy weights off the floor, but I can manage if they are conveniently positioned, e.g. on a table
4 Pain prevents me lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned
5 I can only lift light weights at the most

Section 4: Walking

0 I have no pain walking
1 I have some pain walking, but I can still walk my required, normal distances
2 Pain prevents me from walking long distances
3 Pain prevents me from walking intermediate distances
4 Pain prevents me from walking even short distances
5 Pain prevents me from walking at all

Section 5: Sitting

0 Sitting does not cause me any pain
1 I can sit as long as I need provided I have my choice of sitting surfaces
2 Pain prevents me from sitting more than 1 hour
3 Pain prevents me from sitting more than ½ hour
4 Pain prevents me from sitting more than 10 minutes
5 Pain prevents me from sitting at all

Section 6: Standing

0 I can stand as long as I want without pain
1 I have some pain while standing, but it does not increase with time
2 I cannot stand for longer than 1 hour without increasing pain
3 I cannot stand for longer than ½ hour without increasing pain
4 I cannot stand for longer than 10 minutes without increasing pain
5 I avoid standing because it increases the pain immediately

Section 7: Sleeping

0 I have no pain while in bed
1 I have pain in bed, but it does not prevent me from sleeping well
2 Because of pain I sleep only ¾ of normal time
3 Because of pain I sleep only ½ of normal time
4 Because of pain I sleep only ¼ of normal time
5 Pain prevents me from sleeping at all

Section 8: Social Life

0 My social life is normal and gives me no pain
1 My social life is normal, but increases the degree of pain
2 Pain prevents me from participating in more energetic activities e.g. sports, dancing
3 Pain prevents me from going out very often
4 Pain has restricted my social life to my home
5 I hardly have any social life because of pain

Section 9: Traveling

0 I get no pain while traveling
1 I get some pain while traveling, but none of my usual forms of travel make it any worse
2 I get some pain while traveling, but it does not compel me to seek alternative forms of travel
3 I get extra pain while traveling that requires me to seek alternative form of travel
4 Pain restricts all forms of travel
5 Pain prevents all forms of travel except when performed lying down

Section 10: Employment/Homemaking

- **0** My normal job/homemaking duties do not cause pain
- **1** My normal job/homemaking duties cause me extra pain, but I can still perform all that is required of me
- **2** I can perform most of my job/homemaking duties, but pain prevents me from performing more physically stressful activities e.g. lifting, vacuuming etc.
- **3** Pain prevents me from doing anything but light duties
- **4** Pain prevents me from doing even light duties
- **5** Pain prevents me from performing any job or homemaking chore

Score:_____/50 Transform to percentage score x 100= _____%

Modified Scoring:
Each of the 10 items is scored from 0-5. The maximum score is therefore 50. The obtained score can be multiplied by 2 to produce a percentage score. Occasionally, a respondent will not complete one question or another. The average of all other items is then added to the completed items. Report scores as a percentage.

Appendix 3

General Informed Consent Form
NSU Consent to be in a Research Study Entitled
The effect of dry needling at the thoracolumbar junction on measures of sympathetic outflow and local and remote muscular flexibility in subjects with low back pain and decreased hamstring length

Who is doing this research study?

College: Dr. Pallavi Patel College of Health Care Sciences, Physical Therapy Department

Principal Investigator: Nicole Ginette Clark, PT, MSPT

Faculty Advisor/Dissertation Chair: Cheryl Hill, PT, DPT, PhD

Co-Investigator(s): Joshua Cleland, PT, PhD

Site Information:
Sports and Orthopaedic Therapy Services, LLC
10605 Concord St
Suite 105
Kensington, MD 20895

Funding: Funding will be applied for through the NSU Health Professions Division

What is this study about?

This is a research study, designed to test and create new ideas that other people can use. The purpose of this research study is to understand how trigger point dry needling affects flexibility, as well as one branch of the nervous system. Dry needling has been in the scope of practice for physical therapists in the state of Maryland since 1989, and it is becoming a more common treatment for pain. Currently, there is limited research on how dry needling affects pain, flexibility, and the nervous system. This study will help physical therapists and other health care providers make informed decisions on which treatments to provide their patients.

Why are you asking me to be in this research study?

You are being asked to be in this research study because you have lower back pain along with tightness of at least one hamstring. It has been determined through a preliminary screening that you may be a good candidate for trigger point dry needling for your lower back pain.

This study will include about 54 people.

What will I be doing if I agree to be in this research study?

While you are taking part in this research study, you will be asked to attend 2 sessions on consecutive days (i.e. Saturday and Sunday). The initial session will last approximately 90 minutes, and the follow-up session the following day will last 50 minutes.

Research Study Procedures - as a participant, this is what you will be doing:

Your eligibility will be confirmed after measuring hamstring flexibility. You must have limited flexibility of at least one hamstring to be able to participate. The skin on your back will be examined to make sure you do not have any infections or swelling that would put you at risk for complications with dry needling. You will be attending two sessions for data collection on consecutive days (Saturday and Sunday). After you complete the informed consent and all your questions and concerns have been addressed by the primary investigator, data collection will begin.

You will be randomly assigned to one of two groups. The first group will receive trigger point dry needling to 4 points in the low back, and the second will receive a placebo treatment of dry needling. To determine your group assignment, the primary investigator will select one pre-sealed opaque envelope at the start of your first session. The envelope will contain an index card with your group assignment. Pressure-pain threshold, flexibility measurements, and a pain rating will be collected. A 10-item disability index will be completed. The total time for this will be approximately 20 minutes.

You will then be connected to a machine that will measure activity of a part of your nervous system. All of these tests are non-invasive and should not cause you any pain. A 5-minute baseline measurement will take place. You will then undergo your assigned dry needling treatment (dry needling or placebo). The primary investigator will carefully locate the correct locations for treatment. Four places in your back will be treated for 15 seconds each. Afterward, you will undergo another 5-minute recording. You will be disconnected from the machine, and your flexibility, pressure-pain threshold, and pain rating will be recorded. Combined, these steps will take approximately 70 minutes, for a total of 90 minutes the first day.

You will return the next day, and your flexibility, pressure-pain threshold, and pain rating will be recorded. You will complete the 10-item disability index and a Global Rating of Change, and then you will undergo recording of your nervous system using the same non-invasive tests as your first session. This will total 50 minutes. At this time you will be able to learn to which group you were assigned and if you were part of the placebo group, you will be offered dry needling in the same manner as the other group. If you choose to have dry needling, it will be an additional 10 minutes.

Are there possible risks and discomforts to me?

This research study involves minimal risk to you. This study uses pressure-pain threshold and flexibility testing, which may cause some transient discomfort. Dry needling is an invasive procedure, and there are potential risks. As with any invasive procedure, there is a risk of infection. There have been isolated cases of skin infection, but this is usually a result of negligence or a lack of training by the person providing the treatment. Nicole G. Clark, PT,

MSPT has been trained and certified by KinetaCore® and has met requirements for Level 2 competency in dry needling. The most common complications with dry needling and rates of occurring are: minor brusing (6.7%), minor bleeding (3%), worsening pain (1-2%), and needling pain more than a little sharpness (1%). There can be some discomfort during and after the dry needling. The discomfort during the procedure is moderate and in this study should last no more than 15 seconds with each of 4 areas that are treated. Discomfort after the procedure is mild and lasts approximately a few hours. Serious complications may include accidental puncture of the lung (pneumothorax). The World Health Organization considers a puncture of the lung during dry needling to be "very rare", with a rate of 1 in 70,000 or more treatments. A lung puncture occurs most frequently when areas around the collar bone (clavicle) are treated, and this study does not involve treatment in that area. If this were to occur, it may require a chest x-ray and no further treatment. The symptoms of shortness of breath may last for several days to weeks. A more severe puncture can require hospitalization and re-inflation of the lung. These rates of injury are much lower than those associated with taking over the counter medications, such as ibuprofen, aspirin, and acetaminophen.

Another potential risk of participating in this study is a breach of privacy. A breach of privacy is unlikely to occur because your privacy will be protected in many ways during this research study. All research documents will have your name removed and you will be identified by an assigned code. These documents will be kept in a locked cabinet inside a locked office, and only the primary investigator will have access to these documents. A master list of participants will be kept in a separate locked cabinet within the locked office. Maryland state law requires medical documents to be retained for 5 years, at which time these documents will be destroyed.

What if a research-related injury occurs?

The researchers have taken steps to minimize the known or expected risks. However, you may still have problems or get side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you have a bad reaction, please contact Nicole G. Clark, PT, MSPT right away. See the contact section at the end of this form for phone numbers and more information.

Nova Southeastern University does not have a program to pay you if you are hurt or have other bad results from being in this study. However, medical care at Nova Southeastern University is open to you as it is to all sick or injured people. If you have health insurance, the costs for any treatment or hospital care you receive as result of a study-related injury will be billed to your health insurer. Any costs that are not paid for by your health insurer will be billed to you. If you do not have health insurance, you will be billed for the costs of any treatment or hospital care you receive because of a study-related injury.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed because of participation in this study.

What happens if I do not want to be in this research study?

You have the right to leave this research study at any time, or not be in it. If you do decide to

leave or you decide not to be in the study anymore, you will not get any penalty or lose any services you have a right to get. If you choose to stop being in the study, any information collected about you **before** the date you leave the study will be kept in the research records for 5 years from the conclusion of the study (according to Maryland law) but you may request that it not be used.

What if there is new information learned during the study that may affect my decision to remain in the study?

If significant new information relating to the study becomes available, which may relate to whether you want to remain in this study, this information will be given to you by the investigators. You may be asked to sign a new Informed Consent Form, if the information is given to you after you have joined the study.

Are there any benefits for taking part in this research study?
The possible benefit of your being in this research study is decreased pain and improved flexibility after trigger point dry needling. There is no guarantee or promise that you will receive any benefit from this study. We hope the information learned from this research study will benefit other people with similar conditions in the future.

Will I be paid or be given compensation for being in the study?

You will not be given any payments or compensation for being in this research study.

Will it cost me anything?

There are no costs to you for being in this research study.

Ask the researchers if you have any questions about what it will cost you to take part in this research study (for example bills, fees, or other costs related to the research).

Will clinically relevant research results be shared with me?

The study investigators plan to share certain research results with people who are in the study if they think they are important for you to know. The results will be shared with you in an aggregated format, meaning that the results apply to the groups who participated in the study. The study team will share these results by emailing a summary of group averages along with a description of what the different averages mean. In order to receive this summary you must notify the primary investigator. The summary will be available within 60 days of the conclusion of data collection.

How will you keep my information private?

Information we learn about you in this research study will be handled in a confidential manner, within the limits of the law and will be limited to people who have a need to review this information. You will be given an assigned code, and all study documents that are generated will contain this code instead of your name, or other identifying information. A master list of

participants will be kept separately from the data we collect during this study. Organizations that may review and copy your information include the Institutional Review Board and other representatives of this institution. If we publish the results of the study in a scientific journal or book, we will not identify you. All confidential data will be kept securely in a locked cabinet inside the primary investigator's locked office. All data will be kept for 5 years after the conclusion of the study, in accordance with Maryland law, and will be destroyed after that time by shredding documents with identifying information.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Whom can I contact if I have questions, concerns, comments, or complaints?

If you have questions now, feel free to ask us. If you have more questions about the research, your research rights, or have a research-related injury, please contact:

Primary contact:
Nicole G. Clark, PT, MSPT can be reached at (203)-870-5305.

If primary is not available, contact:
Cheryl Hill, PT, DPT, PhD can be reached at (954)-292-8700.

Research Participants Rights
For questions/concerns regarding your research rights, please contact:

Institutional Review Board
Nova Southeastern University
(954) 262-5369 / Toll Free: 1-866-499-0790
IRB@nova.edu

You may also visit the NSU IRB website at www.nova.edu/irb/information-for-research-participants for further information regarding your rights as a research participant.

All space below was intentionally left blank.

Research Consent & Authorization Signature Section

Voluntary Participation - You are not required to participate in this study. In the event you do participate, you may leave this research study at any time. If you leave this research study before it is completed, there will be no penalty to you, and you will not lose any benefits to which you are entitled.

If you agree to participate in this research study, sign this section. You will be given a signed copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE STATEMENTS LISTED BELOW ARE TRUE:

- You have read the above information.
- Your questions have been answered to your satisfaction about the research.

Adult Signature Section

I have voluntarily decided to take part in this research study.

Printed Name of Participant	Signature of Participant	Date
Printed Name of Person Obtaining Consent and Authorization	Signature of Person Obtaining Consent & Authorization	Date

Appendix 4

PARTICIPANT RESULTS FORM

Baseline:

FTF:

	1	2	3	Mean
cm				

KE: (degrees)

	1 (R_1/R_2)	2 (R_1/R_2)	3 (R_1/R_2)	Mean (R_1/R_2)
Right / Left	/	/	/	/

SLR: (degrees)

	1 (R_1/R_2)	2 (R_1/R_2)	3 (R_1/R_2)	Mean (R_1/R_2)
Right / Left	/	/	/	/

PPT: (kg/cm^2)

	1	2	3	Mean
Medial Hamstrings				
Lateral hamstrings				
Lateral Epicondyle				

Post-treatment:

FTF:

	1	2	3	Mean
cm				

KE: (degrees)

	1 (R_1/R_2)	2 (R_1/R_2)	3 (R_1/R_2)	Mean (R_1/R_2)
Right / Left	/	/	/	/

SLR: (degrees)

	1 (R_1/R_2)	2 (R_1/R_2)	3 (R_1/R_2)	Mean (R_1/R_2)
Right / Left	/	/	/	/

PPT: (kg/cm^2) R / L

	1	2	3	Mean
Medial Hamstrings				
Lateral hamstrings				
Lateral Epicondyle				

Follow-up:

FTF:

	1	2	3	Mean
cm				

KE: (degrees)

	1 (R_1/R_2)	2 (R_1/R_2)	3 (R_1/R_2)	Mean (R_1/R_2)
Right / Left	/	/	/	/

SLR: (degrees)

	1 (R_1/R_2)	2 (R_1/R_2)	3 (R_1/R_2)	Mean (R_1/R_2)
Right / Left	/	/	/	/

PPT: (kg/cm^2)

	1	2	3	Mean
Medial Hamstrings				
Lateral hamstrings				
Lateral Epicondyle				

Appendix 5

Please rate your pain today, 0 = nothing and 10 = worst pain imaginable:

0	1	2	3	4	5	6	7	8	9	10
none										extreme

"With respect to your back pain, how would you compare yourself now to immediately prior to your dry needling treatment?"