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Spinal manipulation does not affect pressure pain thresholds in the absence of neuromodulators: a randomized controlled trial

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ABSTRACT

Background: Measurement of pressure pain threshold (PPT) is a way to determine one of the many potential treatment effects of spinal manipulative therapy.

Objective: To determine how multiple spinal manipulations administered in a single-session affected PPTs at local and distal sites in asymptomatic individuals.

Methods: Participants were randomly assigned into one of three groups: Group one (n = 18) received a lumbar manipulation followed by a cervical manipulation. Group two (n = 17) received a cervical manipulation followed by a lumbar manipulation. The control group (n = 19) received two bouts of five minutes of rest. At baseline and after each intervention or rest period, each participant's PPTs were obtained using a handheld algometer. The PPTs were tested bilaterally over the lateral epicondyles of the humerus and over the mid-bellies of the upper trapezius, lumbar paraspinal, and the tibialis anterior muscles. This study was registered with ClinicalTrials.gov, and its Identifier is NCT02828501.

Results: Repeated-measures ANOVAs and Kruskal–Wallis tests showed no significant within- or between-group differences in PPT. Within-group effect sizes in the changes of PPT ranged from −.48 at the left paraspinal muscles to .24 at the left lateral humeral epicondyle. Statistical power to detect significant differences at α of 0.05 was calculated to be 0.94.

Conclusions: This study suggests that in young adults who do not have current or recent symptoms of spinal pain, multiple within-session treatments of cervical and lumbar spinal manipulation fail to influence PPTs. Changes in PPT that are observed in symptomatic individuals are likely to be primarily influenced by pain-related neuromodulators rather than by an isolated, mechanical effect of spinal manipulation.

KEYWORDS
Neuromodulation; spinal pain; pain mechanisms

Introduction

Spinal manipulative therapy (SMT) is a key intervention used by manual therapists [1,2] who treat painful spinal disorders.[3–7] A robust body of literature suggests that SMT is associated with favorable outcomes;[2,3,5,7] however, when compared to placebo, or no treatment, the overall effect size of clinical improvement following SMT remains modest.[8,9] A clearer understanding of the biomechanical and neurophysiological mechanisms behind SMT will help refine its utilization and improve its effectiveness.[10,11]

As mechanistic research continues to evolve beyond the assessment of local musculoskeletal effects of SMT,[12,13] an emerging body of literature is generating increased interest in the widespread neurophysiologic effects of this intervention. Although numerous theories describing the widespread effects of SMT have been proposed, two specific neurophysiological theories have been gaining support. The first of these theories is that SMT activates the periaqueductal gray area (PAG) in the mid-brain, which would cause a descending inhibition of nociception at the spinal cord.[11,14–16] This generalized descending inhibition is believed to elicit a diffuse or global reduction in pain [15] A second widely supported neurophysiological theory suggests that SMT triggers events occurring in the spinal cord at the dorsal horn [17] corresponding to the spinal level to which the thrust is applied. These events are believed to activate inhibitory inter-neurons which inhibit nociceptive input and lead to a segmental-level specific reduction in pain [17]. While substantive work has been done to study the effects of each of these mechanisms [18–21], there is a paucity of data that addresses the possible interactions of these two proposed mechanisms in response to SMT.

One of the major barriers to studying the interaction of these mechanisms is that variations in individual patient characteristics can alter perceptions of pain which can potentially modulate the effects of SMT. These characteristics include a wide array of pain-related beliefs and physiologic adaptations. Common examples

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that can adversely modulate the effects of SMT include a person's fear avoidance behaviors [22–24], previous experiences of pain [25], high degrees of pain catastrophizing [25,26], altered emotional state [27], and pain chronicity.[28–31] Each of these different phenomena has been shown to either augment or inhibit neurological activity, i.e. they act as neuromodulators and make it difficult to isolate consistent neurophysiologic effects of SMT in individuals across a spectrum of pain reports. Conversely, there is some evidence to suggest that positive beliefs regarding SMT can enhance the effectiveness of the technique. Bishop et al. found that for patients who believed SMT would improve their symptoms, the inclusion of the technique greatly helped to satisfy their expectations of therapy.[32] The wide array of neuromodulators in people who receive SMT for back pain has made it difficult to clarify consistent neurophysiologic effects of SMT. To assist further investigation, a model is needed to evaluate the effects of SMT in the absence of neuromodulators.

The purpose of this study was to determine how multiple spinal manipulations administered in a single-session affected pressure pain thresholds (PPTs) at local and distal sites in asymptomatic individuals. Findings from this study will allow us to address the interaction of the local and global pain inhibiting mechanisms of SMT that operate on the individual in the absence of any neuromodulators. To determine this, we sampled individuals with no history of spinal pain and assessed PPTs before and after they received a combination of lumbar and cervical SMT. This design allowed us to test two null hypotheses. The first hypothesis was that in the absence of neuromodulators, there would be no difference in the local or global PPT pre- and post-intervention. The second hypothesis was that there would be no additive effect on PPT based on the order in which SMT was administered in the absence of neuromodulators.

Methods

Study design

This was a cross-sectional, single-session, randomized control trial design with three independent groups. Each participant attended a single session in which he or she was randomly assigned to receive: (1) lumbar manipulation followed by cervical spine manipulation (Group 1), (2) cervical spine manipulation followed by lumbar spine manipulation (Group 2), or (3) five (5) minutes of supine rest (Control Group).

Participants

This study was conducted on a convenience sample of adults between the ages 18 and 32 with no reports of low back pain or neck pain for at least 1 year were recruited via word of mouth at the University of South Carolina community. Individuals were excluded if they had any contraindications for SMT (Appendix 1), if they were involved in a worker's compensation claim, currently receiving or seeking medical disability, currently pregnant, or taking opiate-based pain medications. Furthermore, after enrollment into the study but prior to any data collection, the participants underwent a cranial nerve screen. We chose to exclude vertebral artery testing and incorporate instead a cranial nerve screening based on part by the findings of Kerry et al. in 2008. [33] They found that there was little evidence to support the construct validity of functional pre-screening testing for the vertebral artery. Instead, they recommended cranial nerve screening for the differential diagnosing of potential internal carotid artery dysfunction. Informed consent was obtained from all participants. This study was approved by the University of South Carolina Institutional Review Board. This study was registered with ClinicalTrials.gov, and its Identifier is NCT02828501.

Experimental protocol – randomization, physical examination, and outcome measures

After consent was obtained, the participant randomly selected an envelope which contained his or her group allocation. Individuals in the control group were given the option of receiving manipulation upon completion of the study to ensure potential benefits of manipulation were made available to everyone.

Once group allocation was determined, each participant underwent a physical examination including assessments of cranial nerve function followed by observation of range of motion of both cervical and lumbar spine. Specifically, in order to test the first cranial nerve, the participant was asked to smell a bottle of cleaning alcohol. In order to test the second cranial nerve, the participant's field of vision was tested. In order to test cranial nerves III, IV, and VI, the participant was asked to follow an object being moved in an 'H' pattern. To test cranial nerve V, the participant sensation was checked on bilateral aspects of the face and was asked to 'clinch' their jaw. To assess the seventh cranial nerve, the participant was asked to puff out their cheeks, raise their eye brows, to smile, and to frown. As the participant was able to hear instructions, cranial nerve VIII was not assessed. The participant was asked to say 'ahh,' cough, and swallow in order to test cranial nerves IX, X, and XII. The participant was finally asked to elevate their shoulders and protrude their tongue in order to assess cranial nerves XI and XII.

Experimental protocol – procedures

An investigator who was masked to the group allocation measured the participants' pre-intervention PPT with a pressure algometer at locally and distally innervated sites of the targeted spinal segments. We chose PPT, which is

defined as 'the least stimulus intensity at which a subject perceives pain [34]' as our outcome measure of interest because this measure has demonstrated reliability [35–37] and is a quantitative method for identifying the presence or absence of central sensitization [28], which is a key response to neuromodulation.[38,39]

Once the pre-intervention PPT measures were obtained, the participants walked into a separate room to receive their first intervention. Initially, individuals in group one received a lumbar manipulation, individuals in group two received a cervical manipulation, and individuals in group three received five minutes of rest while supine. All interventions were performed by the primary investigator who was a licensed physical therapist with over three years of clinical experience performing spinal manipulations and who was blinded to the PPT measurements.

Once the first intervention was performed, the participant went back to the main room to undergo a second set of PPT measurements after which he or she returned to the treatment room to receive the second intervention. Participants in group one then received a cervical manipulation; participants in group two received a lumbar manipulation, while participants in group three once again received a five-minute rest. Once the second intervention was performed, the participants returned to the main room for a final set of PPT measurements. The flow of the study is summarized in Figure 1.

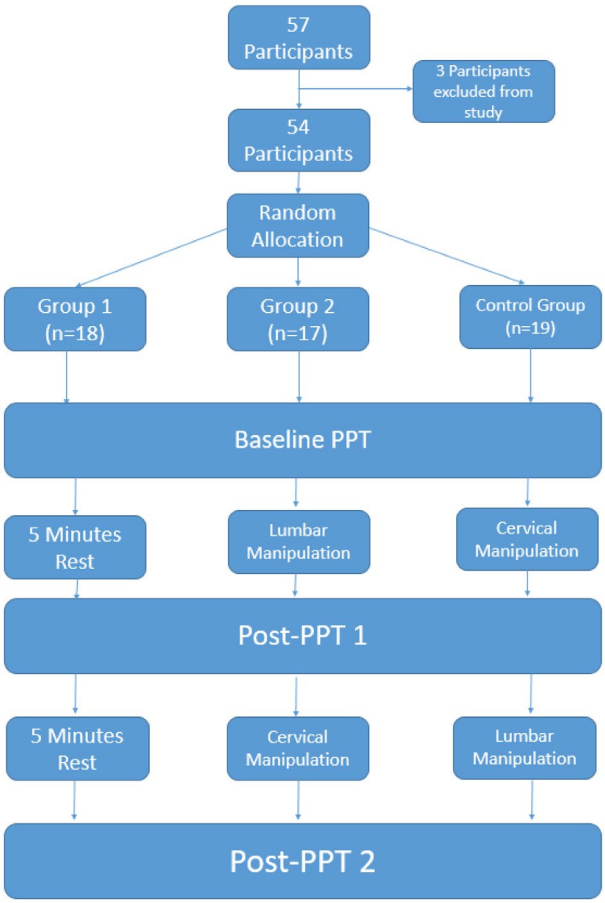

Figure 1. Flow of study.

Mid-cervical spine manipulation

The cervical manipulation was performed as described in Dunning et al., [40]. The participant was positioned supine. Targeting the C4-C5 cervical segment, the clinician placed the lateral aspect of his second middle phalanx on the articular process of the cervical vertebra with the thumb slightly superior to the zygomatic arch. With his stabilizing hand, the clinician supported the base and lateral aspect of the participant's occiput. The clinician positioned the participant's cervical spine in slight extension and adequate ipsilateral side bending and contralateral rotation in order to produce a physiological barrier (Figure 2). He then applied a high-velocity, low amplitude thrust in a diagonal arc to the side of the rotation toward the zygoma with slight superior angulation. If an audible 'pop' or 'cavitation' was not produced on the first attempt, a second attempt was made. A cavitation was perceived by the clinician during either the first or if needed second attempt for all manipulations. The manipulation was then repeated on the contralateral side.

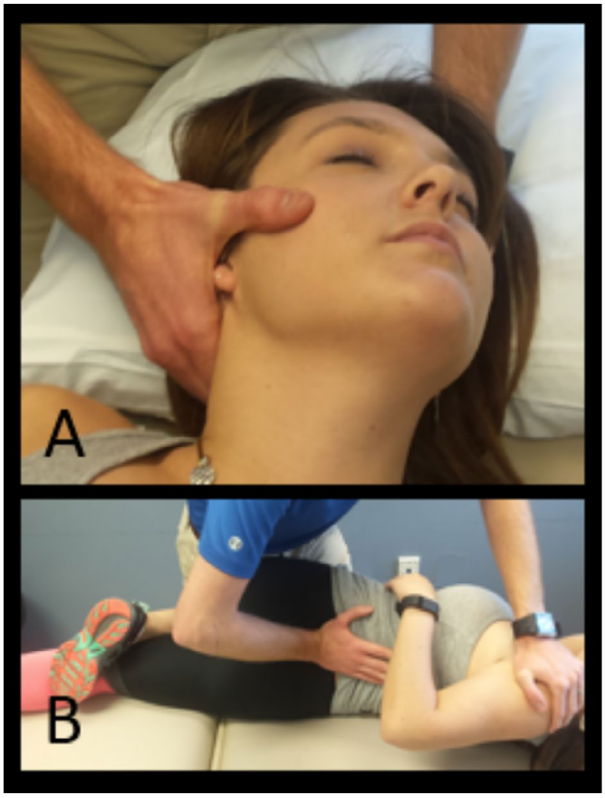

Figure 2. Spinal manipulative treatments. (A) Mid-cervical rotational manipulation. (B) Lower lumbar rotational manipulation.

Lumbar spine manipulation

The lumbar manipulation was performed as described in Beattie et al., [41] With the participant in sidelying, the investigator flexed the participants' right hip and knee

and stabilized the lower extremity by placing the participant's right foot over the popliteal fossa of the left knee. The investigator then pulled the participant's left arm in a medial to lateral direction in order to achieve upper trunk flexion. The participant's left upper extremity was then allowed to rest by his or her side. An anterior and cephalad-directed pressure was then applied with the investigator's right hand contacting the participant's right shoulder. The investigator then maintained contact through the thigh while bringing the participant under his direct line of gravity. The clinician's left hand was positioned later to the L4-L5 interspinous space (Figure 2). A high-velocity, short amplitude thrust was then applied to the targeted segment using the force generated through the thigh contact and the hands. The participant was rotated to the opposite side, and the procedure was repeated. As with the cervical manipulation, if an audible 'pop' or 'cavitation' was not elicited on the first attempt, a second attempt was made. A cavitation was perceived by the clinician during either the first or if needed second attempt for all manipulations.

Measurements of PPT

PPTs were tested at four anatomic locations bilaterally, totaling eight sites. These sites included the lateral epicondyles of the humerus, and the mid-bellies of the upper trapezius, the lumbar paraspinal, and the tibialis anterior muscles. The upper trapezius and lateral epicondyle of the humerus were chosen as measurement sites that may reflect the effects of SMT for the cervical spine manipulation due to their proximity and segmental innervations. Specifically, the upper trapezius was included to assess the C4 dermatome while the lateral epicondyle was chosen to assess the C5 dermatome pattern. Likewise, the lumbar paraspinals and the tibialis anterior measurements were chosen to assess the effects of SMT for the lumbar spine manipulation. The lumbar paraspinals immediately lateral to the L4 spinous process was chosen to assess the effects of the manipulation on the L4 dermatome, and the tibialis anterior was chosen to assess the effects on the L5 dermatome.

Due to our study design, we were able to concurrently use the upper trapezius/lateral epicondyle of the humerus measurements to assess the global effects for SMT of the lumbar spine while using the lumbar paraspinal/tibialis anterior measurements to assess the global effects for SMT of the cervical spine.

Measurements from the upper trapezius and tibialis anterior were obtained from the participant as described by Walton et al. as follows [37]. While in prone, the upper fibers of the trapezius muscle were targeted approximately 5 to 8 cm superior medial from the superior angle of the scapula (Figure 3). Similar to the method described by Koo et al. [42], measures of PPT from the erector spinae muscles were obtained approximately 3 cm lateral from the L4-L5 spinous process (Figure 3). After these

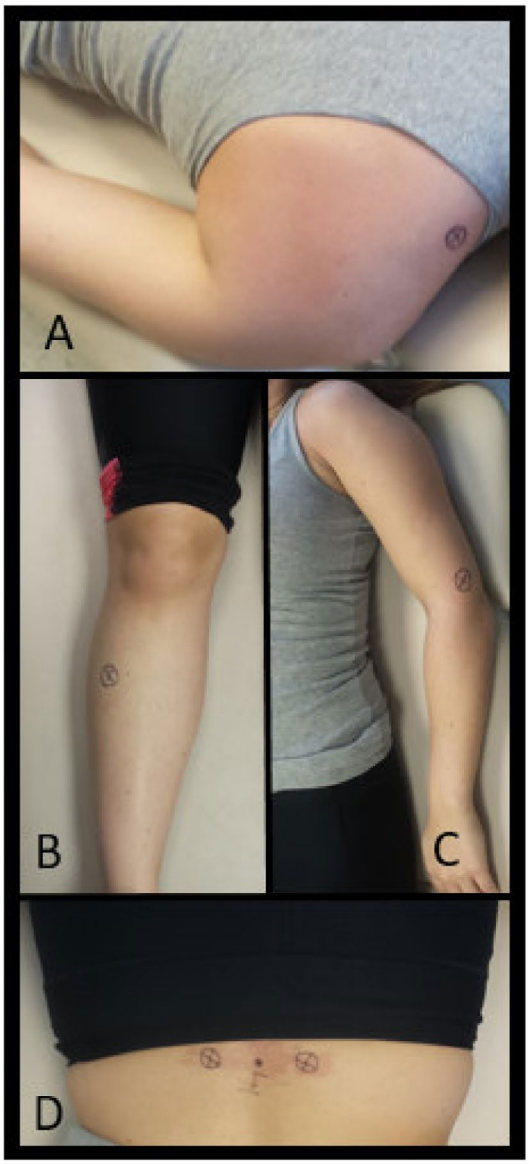

Figure 3. Locations of PPT measurements. (A) Upper trapezius. (B) Tibialis anterior. (C) Lateral epicondyle. (D) Lumbar paraspinals at L4.

measures were obtained, the participants were asked to lie supine for the remaining tests. Measures from the tibialis anterior muscle were obtained approximately 2.5 cm lateral and 5 cm inferior to the tibial tubercle (Figure 3), while the PPTs for the lateral epicondyle were obtained over the most prominent point of the lateral epicondyle (Figure 3). For each measurement, the examiner used the following instructions: 'I am going to begin pressing into your muscle, say "stop" the moment the pressure first changes to unpleasant pain.' We chose the word 'unpleasant' to be in accordance with the definition of pain as dictated by the International Association for the Study of Pain.[43] As described in Walton, the examiner used a rate of 5 N/s (50 kPa/s) when applying the algometer.[37] The same examiner took the PPT measurement in the same order during each assessment in order to reduce error, and a separate examiner recorded the findings in order to eliminate bias. Previous studies have reported

excellent degrees of intra-rater reliability for each of these measures when obtained using this procedure; in all cases, the lower bound of the 95% CI has been shown to exceed .91.[37,39]

Data analysis

Data were analyzed using SPSS version 19 (SPSS and IBM Company, Chicago, IL). Descriptive statistics were calculated for demographic data of all participants. Between-group differences in gender frequency were assessed using chi-square. The distributions of the PPT for each group were tested for assumptions of normality using a Shapiro–Wilk test. Between-group differences in age, height, and weight were determined using a one-way ANOVA with alpha = .05. Power was assessed using G*Power [44] with an alpha of .05, and effect sizes were calculated using Cohen's *d*.[45]

To test our first hypothesis – that in the absence of any neuromodulators, there would be no difference in PPT before or after SMT when applied either locally or distally – we performed a 3 × 3 (group X time) ANOVA comparing the between- and within-group means from the pre- and first post-intervention measurements. Significant *post hoc* comparisons were to be identified using Scheffe's test.

To test our second hypothesis – that in the absence of any neuromodulators, there would be no additive effect of the order or the number of thrusts – we performed a 3×3 (group X time) ANOVA comparing the between- and within-group means from all measurement points. Significant *post hoc* comparisons were to be identified using Scheffe's test. For both our first and second specific aim, if the data violated the assumptions of normalcy, we used a Kruskal–Wallis one-way ANOVA by ranks.

Results

Our results are summarized in Tables 1–4. A total of 57 people (32 = female) with a mean age of 21.71 years (ranging from 18 to 32) participated in this study. Three individuals were excluded from the study. One individual from Group 2 and Group 3 each was excluded for having a higher PPT than our algometer could measure, and one individual in Group 3 or for having an abnormal finding on the cranial nerve screen. There were a total of 19 individuals in the Control Group, 18 individuals in Group 1, and 17 individuals in Group 2 included in the analysis. There were no differences between the groups by gender, ($p = 0.593$), weight ($p = 0.231$), or height ($p = 0.723$).

The results of the 3 × 3 repeated measure ANOVAs and Kruskal–Wallis tests showed no significant within- or between-group differences in PPT. Within-group effect sizes ranged from −.48 at the left low back (pre-intervention to following the first intervention for the second group) to .24 at the left lateral epicondyle (pre-intervention to following the first intervention for the second group). To determine the possibility of statistical misinference due to type II error, we used our lowest effect size, .24, to calculate an additional *post hoc* power analysis using G*Power [44]. Using our sample size of 54 and an α of 0.05, we calculated our overall power to be 0.94, indicating that our study was well-powered.[46]

Discussion

Our findings suggest that in young adult individuals, who are not reporting current or recent pain, spinal manipulation does not result in immediate change in local or global PPTs. The findings in our study are in concordance with those found by Thomson et al. [47]. Using an intervention and measurement protocol similar to ours,

Table 1. Pre- and post-intervention PPTs† over the lumbar paravertebral muscles*.

				95% confidence interval for mean	
Test condition	Group	Mean	SD	Lower bound	Upper bound
Pre-Left Low Back PPT	Control	62.53	22.151	51.85	73.21
	Lumbar	70.21	20.875	59.48	80.94
	Cervical	64.95	17.402	56.29	73.60
Post-1 Left Low Back PPT	Control	50.93	18.859	41.84	60.02
	Lumbar	60.76	21.077	49.92	71.59
	Cervical	57.59	20.187	47.55	67.63
Post-2 Left Low Back PPT	Control	52.08	18.837	43.00	61.16
	Lumbar	67.82	32.698	51.01	84.63
	Cervical	63.88	23.694	52.10	75.66
Pre-Right Low Back PPT	Control	60.94	22.783	49.95	71.92
	Lumbar	67.99	25.892	54.68	81.30
	Cervical	66.33	23.582	54.61	78.06
Post-1 Right Low Back PPT	Control	54.02	20.578	44.10	63.94
	Lumbar	66.56	26.657	52.85	80.26
	Cervical	58.22	21.702	47.42	69.01
Post-2 Right Low Back PPT	Control	54.10	19.678	44.61	63.58
	Lumbar	69.39	29.879	54.02	84.75
	Cervical	65.25	24.965	52.83	77.67

†All measurements are in newtons.
*Measurements were taken 3 cm lateral to the fourth lumbar spinous process.

Table 2. Pre- and post-intervention PPTs† over the lateral epicondyle of the humerus

				95% confidence interval for mean	
Test condition	Group	Mean	SD	Lower bound	Upper bound
Pre-left lateral epicondyle PPT	Control	51.82	16.63	43.80	59.83
	Lumbar	55.47	18.96	45.72	65.22
	Cervical	48.33	17.40	39.68	56.98
Post-1 left lateral epicondyle PPT	Control	46.18	16.16	38.39	53.97
	Lumbar	50.51	22.98	38.69	62.32
	Cervical	46.6	14.44	39.42	53.78
Post-2 left lateral epicondyle PPT	Control	43.66	13.95	36.94	50.39
	Lumbar	49.48	19.93	39.23	59.72
	Cervical	46.24	16.44	38.07	54.42
Pre-right lateral epicondyle PPT	Control	50.05	19.38	40.71	59.39
	Lumbar	58.62	19.93	48.38	68.87
	Cervical	47.55	12.86	41.15	53.94
Post-1 right lateral epicondyle PPT	Control	48.76	13.73	42.14	55.37
	Lumbar	49.41	20.28	38.98	59.84
	Cervical	48.11	14.35	40.98	55.25
Post-2 right lateral epicondyle PPT	Control	48.13	19.03	38.96	57.30
	Lumbar	53.61	25.26	40.62	66.67
	Cervical	46.24	16.03	38.27	54.21

†All measurements are in newtons.

Table 3. Pre- and post-intervention PPTs† over the upper trapezius muscle.

				95% confidence interval for mean	
Test condition	Group	Mean	SD	Lower bound	Upper bound
Pre-left upper trapezius PPT	Control	38.8	16.2	30.99	46.61
	Lumbar	44.48	13.85	37.36	51.6
	Cervical	37.91	11.57	32.16	43.67
Post-1 left upper trapezius PPT	Control	37.71	14.49	30.72	44.69
	Lumbar	47.49	17.67	38.41	56.57
	Cervical	37.39	9.185	32.82	41.96
Post-2 left upper trapezius PPT	Control	40.25	15.15	32.95	47.55
	Lumbar	48.46	21.62	37.34	59.58
	Cervical	39.35	10.98	33.89	44.81
Pre-right upper trapezius PPT	Control	44.04	17.02	35.84	52.24
	Lumbar	48.71	17.64	39.64	57.77
	Cervical	41.28	14.29	34.17	48.38
Post-1 right upper trapezius PPT	Control	41.76	16.15	33.98	49.54
	Lumbar	49.57	18.55	40.05	59.09
	Cervical	44.42	15.81	36.56	52.29
Post-2 right upper trapezius PPT	Control	43.68	18.54	34.75	52.62
	Lumbar	54.91	25.26	41.92	67.89
	Cervical	42.57	11.8	36.7	48.44

†All measurements are in newtons.

Table 4. Pre- and post-intervention PPTs† over the tibialis anterior muscle.

				95% confidence interval for mean	
Test condition	Group	Mean	SD	Lower bound	Upper bound
Pre-left tibialis anterior PPT	Control	58	16.46	50.07	65.94
	Lumbar	62.95	21.65	51.82	74.09
	Cervical	61.45	20.49	51.26	71.64
Post-1 tibialis anterior PPT	Control	56.3	16.76	48.22	64.38
	Lumbar	59.04	19.33	49.1	68.98
	Cervical	62.93	23.58	51.21	74.66
Post-2 tibialis anterior PPT	Control	57.9	17.87	49.29	66.51
	Lumbar	62.56	20.23	52.16	72.96
	Cervical	64.38	24.37	52.26	76.5
Pre-tibialis anterior PPT	Control	60.71	18.80	51.65	69.77
	Lumbar	65.59	18.49	56.08	75.1
	Cervical	65.78	23.32	54.18	77.38
Post-1 tibialis anterior PPT	Control	57.92	20.5	48.06	67.77
	Lumbar	66.28	26.34	52.74	79.83
	Cervical	61.48	17.98	52.54	70.42
Post-2 tibialis anterior PPT	Control	56.99	17.95	48.34	65.65
	Lumbar	68.73	27.36	54.67	82.8
	Cervical	63.14	24.80	50.81	75.47

†All measurements are in newtons.

these authors found that in 50 asymptomatic individuals, neither manipulation nor mobilization to the lumbar spine exhibited a statistically significant increase in PPT.

Interestingly, however, our findings are in direct contrast with others [48–50] that have examined PPTs in asymptomatic people undergoing SMT. Fernandez-de-las-Penas [49] reported that cervical spine manipulation led to an immediate increase in PPT over the lateral epicondyles of the humerus in asymptomatic participants. One reason for this disagreement between this study and ours may be methodologic, i.e. these authors utilized an average of three separate readings, whereas we used only a single measure. We chose to use just a single reading because of the potential sensitizing effect of multiple measures in a short period of time.[51]

In a separate sample, Fernandez-de-las-Penas and colleagues [48] found that after a cervicothoracic manipulation, there were immediate increases in PPT over the C5-C6 zygapophyseal joint. These data may differ from ours due to the fact that they utilized a different manipulation technique and took the PPT over a different area. Finally, Ruiz-Saez et al. in 2007 [50] reported that in asymptomatic individuals, PPTs increased over latent, or asymptomatic, trigger points in the upper trapezius following a cervical manipulation. This sample may differ from ours in that it violates our assumption of individuals presenting with no neuromodulators, as even though the participants are pain-free the presence of trigger points, even latent, may indicate that changes have occurred at the tissue level.

The literature for changes in PPT following SMT is more consistent when individuals with current pain are included. Multiple studies examining changes in pain thresholds in individuals with low back pain [18,52], neck pain [20,53–55], and lateral epicondylitis [56,57] have found consistent increases in PPT from spinal manipulation. These findings, along with our own, could suggest that SMT has a stronger effect on the influences of the neuromodulators associated with pain than the actual nociceptive input itself.

One key marker of neuromodulator that has been investigated in the pain threshold literature is central sensitization. Central sensitization is a phenomenon whereby after repeated activation, the nociceptive system lowers its threshold for activation, allowing normally innocuous stimuli to produce nociception.[51] A key contributor to central sensitization specific to the spinal cord is a C-fiber-mediated phenomenon called temporal summation.[58]

When a painful stimulus of unchanging intensity is repeatedly and rapidly presented to an individual, i.e. temporal summation, he or she will perceive the same stimulus as increasingly painful. While temporal summation is enhanced in people in a painful state [59], this C-fiber-mediated pain is not necessarily limited to the chronic pain population. Bialosky et al. have investigated the effects of spinal manipulation on temporal summation in both healthy [19] and painful individuals [18] using thermal pain thresholds. They found that in both groups, the temporal summation was mitigated by SMT. Further work is needed to elucidate whether SMT can reduce pain perception in the presence of other specific neuromodulators.

Limitations

A limitation to the external validity of our findings is that our sample participants were all in their third decade of life; thus, our data may not generalize to younger or older individuals. A second limitation is that all PPTs were obtained within an approximate 20-min time frame between the initial PPT and the final PPT; thus, we are unable to determine any longer-term effects of SMT on PPT. Since our participant population included only individuals with no current or recent history of spinal pain, we are unable to correlate our findings with changes in pain scores.

Another potential limitation to our study is that we did not exclude individuals who had a history of low back pain beyond the previous year. This threatens the internal validity of our study by the possibility that an individual who has a history of low back pain would continue to have neuromodulators even in the absence of pain. However, a recent study by Ceko et al. [60] found that following successful treatment of low back pain, changes in an individual's central nervous system were normalized. Specifically, they found that intrinsic connectivity of cognitive networks was partially restored following successful treatment. This could suggest that even if the participant did have a history of low back pain, neuromodulation that occurred at that time would be normalized after a long period of symptom relief. Also, we did not account for any neuromodulation that might have occurred due to negative or positive attitudes toward spinal manipulation.

Masking the type of treatment and order in which they were administered was not possible for the participant or the clinician providing the intervention. However, great effort was made to ensure that the investigators collecting and recording the PPT measurements were masked to the treatment and order, and the clinician providing the intervention was blinded to the PPT measurements. Additionally, no effort was made in order to ascertain whether latent trigger points were present at any of the PPT sites.

Conclusions

This study suggests that in young adults who do not have current or recent symptoms of spinal pain, multiple within-session treatments of cervical and lumbar spinal manipulation fail to influence PPTs. Our study provides

a framework for investigating the effects of SMT on both the local and global mechanisms of pain reduction in the absence of any neuromodulators. Further work needs to be done to address how SMT at multiple levels affects pain perception in the presence of specific neuromodulators.

Disclosure statement

No potential conflict of interest was reported by the authors.

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There was no source of funding or other financial support for this study.

Notes on contributors

Max Jordon is a PhD Candidate at the University of South Carolina. He is currently interested in pain modulation and appreciation.

Paul Beattie is a clinical faculty at the University of South Carolina. HE is interested in low back pain research, specifically regarding imaging of the spine and fMRI.

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Appendix 1

Contraindications for Spinal Manipulative Therapy Used in our Study.
The presence of any of the following factors will exclude the subject from this study:

(1) Currently involved in a worker's compensation claim or in personal injury litigation.
(2) Currently on, or applying for, permanent or temporary disability due to a medical or mental health condition.
(3) Activity-limiting pain arising from any site other than listed in the specific entry criteria.

Additional exclusion criteria include the presence of any of the following conditions as determined by prior medical and/or radiographic examination or initial MRI:

- pregnancy;
- spinal osteoporosis;
- inflammatory joint disease;
- any current (within 5 years) neoplastic condition;
- any history of vertebral fracture with current bony instability or measurable deformity;
- severe lumbar stenosis (defined as an A-P diameter of the thecal sac of less than 5 mm at any level, from mid-sagittal lumbar T_2-weighted MRI);
- diagnosis of cervical spinal stenosis;
- any abnormalities or compression of the spinal cord, cauda equine, or spinal nerves;
- any upper or lower extremity nerve impairment;
- unstable angina, congestive heart failure, orthopnea, or severe hypertension;
- any history of a surgical procedure to the cervical or thoracic or lumbar spine;
- any surgical procedures to the abdomen, thorax, upper extremities, head, or neck in the past 6 months prior to enrollment in the study;
- history of whiplash in the last 6 weeks;
- evidence of central nervous system involvement, to include hyperreflexia, sensory disturbances, unsteadiness during walking, nystagmus, loss of visual acuity, impaired sensation of the face, altered taste, abd the presence of pathological reflexes (i.e. positive Hoffman's and/or Babinski reflexes);
- resting blood pressure greater than 140/90 mm Hg at initial intake;
- the presence of any of the following atherosclerotic risk factors: hypertension, diabetes, heart disease, stroke, transient ischemic attack, peripheral vascular disease, smoking, hypercholesterolemia, or hyperlipidemia;
- current use of any of the following medications: opiate-based analgesics, prescribed anticoagulants (this does not include low doses of ASA or NSAIDs), and oral or injected corticosteroids.