

Association of spinal manipulative therapy with changes in cervical motion segment interactions in neck pain patients: An observational study with matched healthy controls

Abstract

Objective

The aims of this study were to determine 1) if intra-regional, inter-vertebral range of motion (IV-RoM) and laxity relationships (associations between 2 separate motion segments within the region of the cervical spine) exist during cervical motion, 2) if there are differences between neck pain and asymptomatic subjects; and 3) if there is any effect of cervical manipulation on these relationships.

Methods

Twenty-nine patients with sub-acute or chronic neck pain, and 33 healthy controls were imaged during flexion and extension, pre and post a course of cervical chiropractic manipulation (patient group only), using a standardised quantitative fluoroscopy acquisition protocol.

Results

Significant correlations between IV-RoMs were found in both neck pain and neck pain free populations at baseline and follow up. Positive relationships were found between (C2-C3 and C3-C4) and (C4-C5 and C5-C6) IV-RoM in both populations. A negative correlation was found in the patient group at baseline between (C1-C2 and C5-C6), but not at follow up. Significant relationships were also found for segmental laxity, with a negative correlation found at (C1-C2 and C5-C6) in the patient group only and at baseline only.

Conclusion

Relationships were found between both intra-regional IV-RoM and laxity, some of which were present in both groups at baseline and follow up, suggestive of 'normal' kinematic behaviours. Changes in correlations unique to the patient group, may be indicative of a change in regional kinematics resulting from the manipulation intervention.

Introduction

Spinal manipulative therapy (SMT) is recommended by clinical practice guidelines ^(1, 2) and commonly sought in the treatment of neck pain ⁽³⁾ however, its mechanisms of action remain unclear ⁽⁴⁾. Whilst biomechanical models are typically offered as the primary basis for the mechanistic explanation of manipulation ⁽⁵⁾, the therapeutic effects of manipulation are believed to be mediated by mechanical, neurophysiological and psychological mechanisms ^(6, 7). As a mechanical stimulus, it is proposed that SMT sets off a chain of neurophysiological and psychological responses that account for the clinical outcomes ⁽⁸⁾, however this literature is typically limited by the use of cadavers, animal models, and the use of asymptomatic volunteers, which limits the applicability of findings to the clinical scenario. In addition, previous research infrequently includes a control group, and the focus has been the lumbar spine, which is biomechanically distinct from the cervical spine ⁽⁹⁾.

A mechanical consequence of SMT is believed to be changes in inter-vertebral ranges of motion (IV-RoM) and subsequently regional ranges of motion. There is evidence to suggest that SMT increases regional cervical ranges of motion ⁽¹⁰⁻¹³⁾, however little is known about cervical inter-vertebral movement in asymptomatic controls or changes in motion associated with interventions such as SMT, in patient groups. Whilst several regional measurement tools have been shown to be reliable and accurate for use in the cervical spine ^(14, 15), such systems are perhaps best utilised at the group

level as their utility at the individual patient level is less certain⁽¹⁶⁾, and they cannot assess inter-vertebral motion directly.

Spinal manipulative therapy is directed towards and attempts to affect inter-vertebral function, and so any exploration into the mechanisms of action of SMT should arguably be conducted at the inter-vertebral level. It has been shown that it is possible to measure intervertebral kinematic variables in the cervical spine using Quantitative Fluoroscopy (QF)⁽¹⁷⁾. Quantitative Fluoroscopy represents an advance over traditional flexion-extension radiography, as it allows kinematic parameters to be measured throughout the motion sequence and not just at the end-range. Therefore, the true maximal inter-vertebral range of motion (IV-RoMmax) reached during a movement may be measured, even if it does not occur at the end-range of regional spinal motion^(17, 18). In a study that utilised QF, there were no statistically significant differences in cervical flexion-extension IV-RoMmax between patients with neck pain and healthy controls nor in the prevalence of hypomobile segments (motion at or below the 2.5th percentile for that segment). In addition, the number of flexion-extension hypomobile segments was unchanged in neck pain patients post-SMT.

Quantitative Fluoroscopy allows for the measurement of other variables and because measurement is continuous throughout a motion cycle, it is possible to calculate laxity. Segmental laxity has been proposed as a surrogate indicator of the inter-vertebral neutral zone⁽¹⁹⁾. A previous investigation into IV-RoMmax and segmental laxity of the lumbar spine during sagittal bending in non-low back pain participants showed that there is a likely co-dependence between motion segments during such movements in terms of both IV-RoMmax and laxity⁽²⁰⁾. That study suggested that the IV-RoMmax's of L2-L3 and L3-L4 were positively correlated (i.e. if the range of movement at L2-L3 increased, so did the range of motion at L3-L4). However, the ranges of motion at both these levels was shown to be negatively associated with L4-L5 range, and with the degree of laxity at this level, suggesting that a compensatory mechanism exists between motion segments.

Such relationships have never been investigated in the cervical spine. It is also not known how treatment interventions such as SMT might affect such segmental interactions. Therefore, the objectives of this study were to determine:

- 1) if IV-RoMmax and laxity interactions exist in the cervical spine during flexion;
- 2) if there are differences in IV-RoMmax or laxity parameters between baseline and follow up in both patients with neck pain and asymptomatic healthy controls; and
- 3) if there is an effect on IV-RoMmax/laxity relationships in patients with neck pain after SMT.

Methods

Study Design

This was an observational study of patients with non-specific neck pain receiving SMT and matched, untreated healthy controls as a reference group.

Participants

Thirty patients aged 18-70 years with at least 2 weeks of non-specific neck pain rated 3 or above on the 11-point numerical rating scale were recruited from an outpatient teaching clinic, prior to receiving any treatment. Recruitment took place between August 2011 and April 2013. An equal number of pain-free healthy controls were recruited from university staff, students and visitors, who

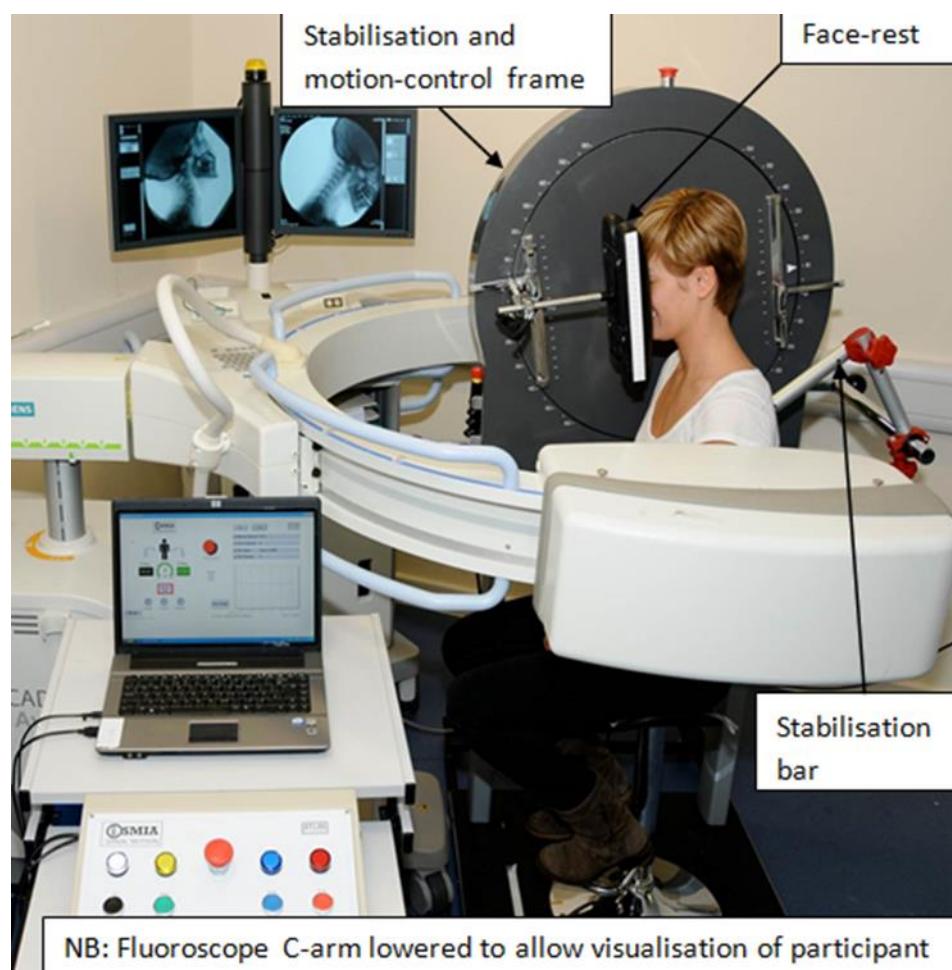
were age and gender-matched to patients. Details regarding exclusion criteria have been previously published⁽¹⁷⁾. Briefly, participants were excluded if they had a history of cervical spine surgery, depression, poor understanding of English, were currently involved in another research study or if X-ray exposure was contraindicated for any reason. Controls were required to have not experienced activity-limiting neck pain lasting more than 24 hours in the past 12 months and have no current neck pain, dizziness, or vertigo (unsteadiness). Patients underwent a standard case history and examination by a final year chiropractic student intern and a chiropractor. Patients had 8 treatment visits scheduled (twice weekly over 4 weeks) for SMT (consisting of high-velocity, low-amplitude adjustments directed at a level determined by the practitioner at the treatment visit). Ethical approval was granted by the UK National Research Ethics Service South West – Cornwall and Plymouth (11/SW/0072). All participants provided consent.

Data collection

Imaging sequence acquisition and analysis

All participants had cervical intervertebral motion measured in flexion and extension by QF at baseline and 4-week follow-up using a standardised protocol which is described in more detail elsewhere⁽¹⁷⁾. In brief, participants were seated and instructed to follow a face-rest attached to a motorised motion-frame which guided them through their maximum flexion and return to neutral at a standardised rate and over a standardised range (Figure 1).

Figure 1: Fluoroscope and motion frame configuration



Participants' cervical spine motion was simultaneously imaged using a digital fluoroscope. On the first image of each sequence with the spine in neutral, templates were manually positioned to register the position of each cervical vertebra. Thereafter vertebral positioning was tracked throughout the motion sequence using bespoke frame-frame codes written in Matlab (V2013 – the Mathworks Inc.). Laxity was calculated as the ratio of the slopes of neck motion to intervertebral motion during the first 10° of neck bending⁽²⁰⁾. IV-RoMmax was calculated from C1-2 to C5-6 using a method previously described elsewhere⁽²¹⁾. The accuracy of QF measurement of cervical IV-RoMmax has been determined as 0.5° for flexion and 0.4° for extension⁽¹⁷⁾. The inter-observer repeatability of cervical spine QF has been demonstrated as excellent with agreement (standard errors of measurement) between 0.3 and 1.1° and reliability (intraclass correlation coefficients) between 0.90 and 0.99 depending on level⁽¹⁷⁾.

Data analysis

The normality of data distributions was assessed with the Shapiro-Wilk test. Means for each of the continuous variables from control and patient groups were analysed for differences using the unpaired Student's t test. Relationships between the IV-RoMmax at each individual motion segment and all other motion segments within the region of (C1-C6) were analysed using either a Pearson's Correlation Coefficient or Spearman's rank correlations dependent on the whether the data were normally distributed or not. This analysis was repeated for the inter-segmental laxity data. Correlation coefficients were interpreted as follows: 0.0-0.1 Negligible; 0.10 – 0.39 Weak; 0.40 – 0.69 Moderate; 0.70-0.89 Strong; 0.9 – 1.0 Very Strong⁽²²⁾.

Results

Sixty-one (33 healthy controls) adults satisfied the inclusion criteria and provided consent to participate. Participant demographic data has previously been published elsewhere⁽¹⁷⁾. In brief, the mean age of patients was 40 (SD:13.1) years and 70% were female. The mean baseline pain intensity NRS/10 score was 5 (1.5), and mean NDI/50 was 13 (6.7). Due to template tracking failures, final group sizes for inclusion in analysis of were control group n = 28, and patient group n = 27 for baseline and follow up respectively for IV-RoMmax calculations. For laxity calculations, the data supported outputs for the control group n = 32 at baseline and n = 33 at follow up and for the patient group n = 28 for both baseline and follow up (laxity calculations). Mean radiation dose for participants was 0.013mSv. The inter-vertebral flexion ranges of motion for each segment are provided in Table 1. None of the differences within or between groups were statistically significant except for C3-C4 which on average increased in range by 1.2° at follow-up in patients (p = 0.01, 95%CI 0.2 – 2.2°). It is noted however that this change is only marginally above the standard error of measurement.

Table 1: Inter-vertebral flexion ranges of motion in degrees (IV-RoMmax)

Motion Segment		Control Group	Patient Group	Difference (95% CI)
		Mean (SD)	Mean (SD)	
C1-C2	Baseline	7.4 (3.5)	7.7 (3.7)	-0.4 (-2.3 to 1.6)
	Follow-up	8.0 (3.9)	6.8 (3.3)	
	Difference (95% CI)	-0.6 (-1.7 to 0.4)	-0.9 (-1.9 to 0.1)	
C2-C3	Baseline	5.9 (2.8)	5.6 (3.1)	0.2 (-1.3 to 1.9)
	Follow-up	5.7 (2.6)	6.2 (2.7)	

	Difference (95% CI)	0.2 (-0.7 to 1.0)	0.6 (-0.4 to 1.5)	
C3-C4	Baseline	6.6 (2.8)	6.9 (3.8)	-0.3 (-2.1 to 1.4)
	Follow-up	7.1 (2.9)	8.1 (3.3)	
	Difference (95% CI)	-0.5 (-1.4 to 0.5)	1.2 (0.2 to 2.2)	
C4-C5	Baseline	6.1 (3.4)	5.8 (2.8)	0.3 (-1.5 to 1.8)
	Follow-up	6.2 (3.1)	6.7 (3.2)	
	Difference (95% CI)	-0.1 (-0.8 to 0.6)	0.9 (-0.1 to 1.9)	
C5-C6	Baseline	5.8 (3.8)	4.9 (2.9)	0.9 (-1.2 to 2.8)
	Follow-up	5.8 (3.2)	5.6 (2.6)	
	Difference (95% CI)	0.02 (-0.7 to 0.8)	0.7 (-0.6 to 2.2)	

SD, standard deviation; 95% CI, 95% Confidence Interval

The inter-vertebral laxity indices in flexion are provided in Table 2. The only significant difference between or within groups was C1-C2 which was smaller in patients at baseline and, at follow-up, increased in patients only.

Table 2: Inter-vertebral flexion laxity indices

Motion Segment		Control Group Mean (SD)	Patient Group Mean (SD)	Difference (95% CI)
C1-C2	Baseline	0.160 (0.1361)	0.092 (0.0933)	0.068 (0.0066 to 0.1300)
	Follow-up	0.144 (0.1412)	0.143 (0.0990)	
	Difference (95% CI)	-0.422 (-0.1157 to 0.0312)	0.055 (0.0032 to 0.1062)	
C2-C3	Baseline	0.129 (0.0586)	0.118 (0.0762)	0.011 (-0.0253 to 0.0462)
	Follow-up	0.130 (0.06882)	0.125 (0.7609)	
	Difference (95% CI)	0.005 (-0.2884 to 0.0389)	0.004 (-0.0367 to 0.0453)	
C3-C4	Baseline	0.164 (0.1120)	0.137 (0.0788)	0.027 (-0.0246 to 0.0773)
	Follow-up	0.171 (0.1085)	0.138 (0.0779)	
	Difference (95% CI)	-0.017 (-0.07631 to 0.0419)	-0.001 (-0.0438 to 0.0408)	
C4-C5	Baseline	0.140 (0.0714)	0.127 (0.0894)	0.013 (-0.0292 to 0.0550)
	Follow-up	0.127 (0.0846)	0.148 (0.0947)	
	Difference (95% CI)	-0.017 (-0.0601 to 0.0253)	0.019 (-0.0302 to 0.0697)	
C5-C6	Baseline	0.106 (0.0876)	0.092 (0.0828)	0.014 (-0.0307 to 0.0578)
	Follow-up	0.102 (0.0818)	0.109 (0.0782)	
	Difference (95% CI)	-0.025 (-0.0717 to 0.0211)	0.014 (-0.0291 to 0.0578)	

SD, standard deviation; 95% CI, 95% Confidence Interval

Correlations IV-RoMmax

An overview of the correlations found between IV-RoMmax at different segmental levels is provided in Table 3. In both groups at both baseline and follow-up moderate correlations were exhibited between C2-C3 and C3-C4 (r 0.490 to 0.596), and between C4-C5 and C5-C6 (r 0.433 to 0.677). The only negative coefficient that indicated (at least) moderate correlation was that of C1-C2 and C5-C6 in the patient group at baseline ($r=0.427$) (Figure 2C). This correlation was no longer present at follow-up (Figure 2D).

Table 3: Inter-motion segment relationships (IVRoMmax)

Motion	Segment	Control Group		Patient Group	
		Pair	Baseline n= 28	Follow-up n = 28	Baseline n = 27
C1-C2	C2-C3	r_s value	0.154	0.009	0.13
		p value	.435	.963	.518
C1-C2	C3-C4	r_s value	0.311	0.088	0.222
		p value	.107	.656	.267
C1-C2	C4-C5	r_s value	0.511	0.317	0.055
		p value	.005**	.1	.785
C1-C2	C5-C6	r_s value	0.342	0.292	-0.427
		p value	.075	.132	.026*
C2-C3	C3-C4	r_s value	0.596	0.49	0.596
		p value	.001**	.008**	.002**
C2-C3	C4-C5	r_s value	0.38	0.308	0.213
		p value	.046*	.111	.286
C2-C3	C5-C6	r_s value	0.144	0.145	-0.096
		p value	.465	.462	.634
C3-C4	C4-C5	r_s value	0.327	0.226	0.484
		p value	.089	.247	.01**
C3-C4	C5-C6	r_s value	0.107	-0.049	-0.135
		p value	.589	.806	.502
C4-C5	C5-C6	r_s value	0.677	0.512	0.433
		p value	.00**	.005**	.024*

r_s value = Spearman's rank correlation coefficient

* = $p < .05$ ** = $p < .01$

Figure 2 (A-D): Scatter Plots showing IVRoM correlations between the levels of C1-C2 and C5-C6 in controls and patients at baseline and follow up

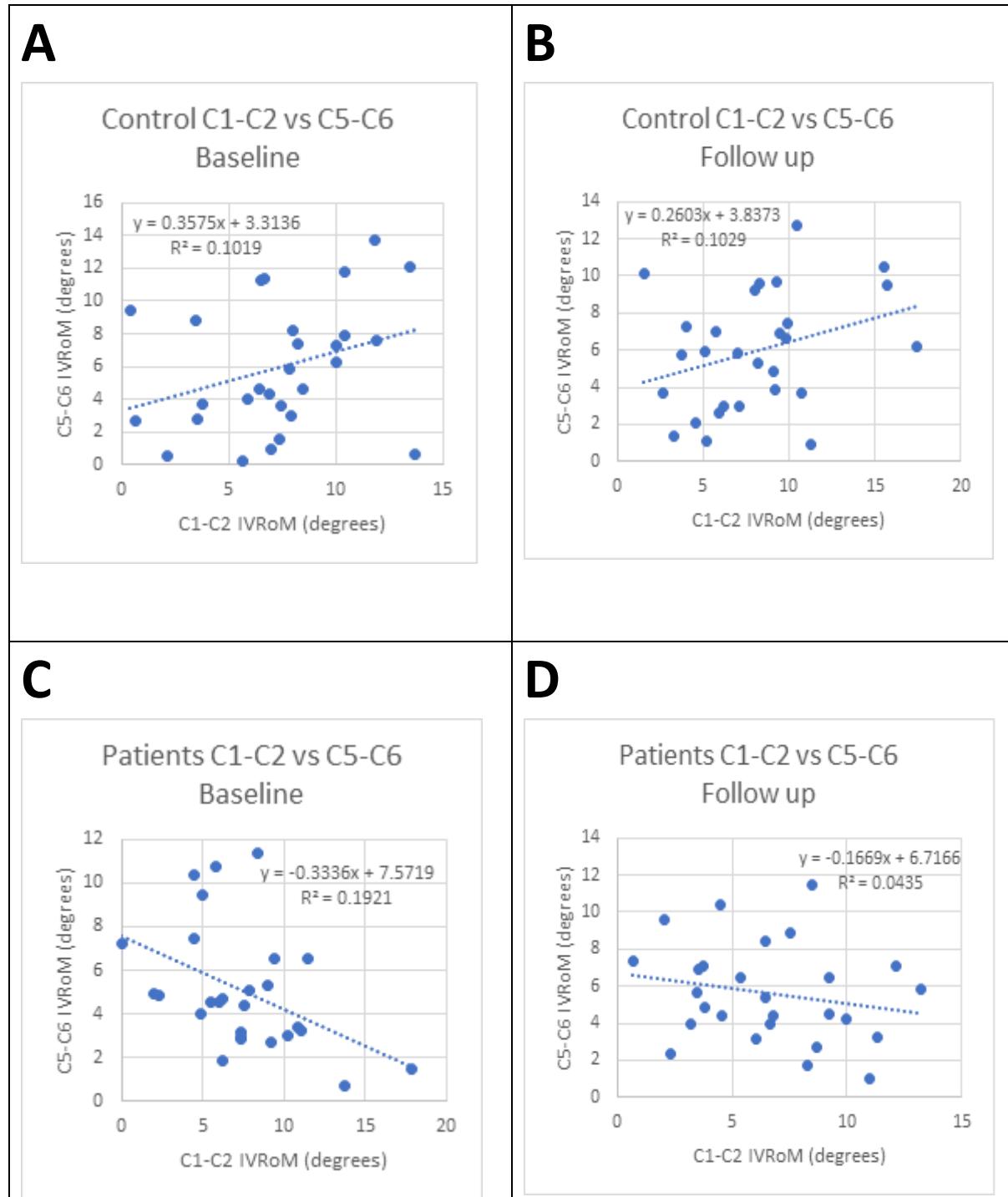


Figure 2 shows the relationships between the IVRoMmax of C1-C2 and C5-6. In controls there was a weak positive correlation at baseline (A) which remained unchanged at 4-week follow-up (B). In contrast the relationship between these segments in patients was moderately negatively correlated at baseline (C), while at 4-week follow-up the correlation was weak to negligible (D).

Inter-motion segment relationships (laxity)

An overview of the correlations found between laxity at different segmental levels is provided in Table 4. The correlations for laxity at different segmental levels were also calculated at baseline and follow up for both groups. In the control group, moderate correlations were shown between C2-C3 and C3-C4 and C4-C5 and C5-C6 at baseline, and between C1-C2 and C5-C6 (Figure 3B), and C2-C3 and C3-C4, at follow-up. In the patient group moderate correlations were shown between (C2-C3 and C3-C4) at baseline, and between C1-C2 and C2-C3, and C2-C3 and C5-C6 at follow up. A moderate negative correlation was shown in the patient group only at baseline between C1-2 and C5-6 (Figure 3C). This relationship was no longer present at follow up (Figure 3D).

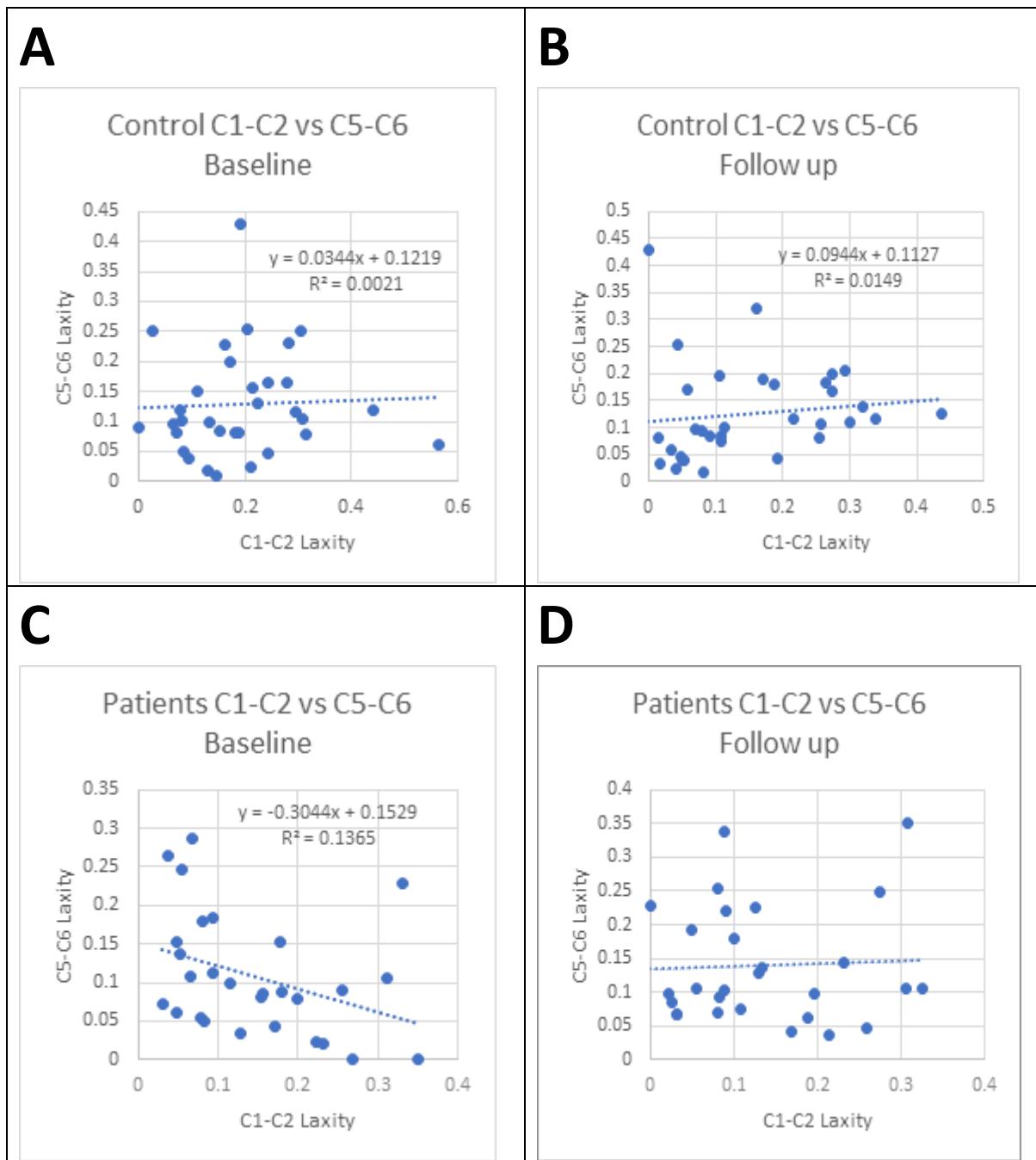
Table 4: Inter-motion segment relationships (laxity)

Motion Segment Pair		Control Group		Patient Group	
		Baseline n = 32	Follow-up n = 33	Baseline n = 28	Follow-up n = 28
C1-C2	C2-C3	r value	0.144 (r_s)	0.142	0.42
		p value	.433	.273	.026*
C1-C2	C3-C4	r value	0.078 (r_s)	0.16	0.381 (r_s)
		p value	.672	.317	.045*
C1-C2	C4-C5	r value	0.288	0.007 (r_s)	0.027
		p value	.11	.336	.893
C1-C2	C5-C6	r value	0.206 (r_s)	-0.415	0.273
		p value	.258	.011*	.16
C2-C3	C3-C4	r value	0.453 (r_s)	0.397	0.314 (r_s)
		p value	.009**	.036*	.103
C2-C3	C4-C5	r value	0.361 (r_s)	0.183 (r_s)	0.078
		p value	.042*	.352	.694
C2-C3	C5-C6	r value	0.189 (r_s)	-0.049	0.512
		p value	.3	.413	.005**
C3-C4	C4-C5	r value	0.334 (r_s)	0.032 (r_s)	0.251 (r_s)
		p value	.061	.109	.198
C3-C4	C5-C6	r value	0.069 (r_s)	0.134	-0.008 (r_s)
		p value	.706	.497	.969
C4-C5	C5-C6	r value	0.403 (r_s)	0.074 (r_s)	0.227
		p value	.022*	.71	.245

r_s value = Spearman's rank correlation coefficient

* = $p < .05$ ** = $p < .01$

Figure 3 (A-D): Scatter plots showing laxity correlations between the levels of C1-C2 and C5-C6 in controls and patients at baseline and follow up.



In Figure 3 can be seen the relationships between the laxity indices of C1-C2 and C5-C6. In controls there was a weak positive correlation at baseline (A) which remained positive (moderate correlation) at 4-week follow-up (B). In contrast the relationship between these segments in patients was moderately negatively correlated at baseline (C), but at 4-week follow-up the correlation was weak (D).

Discussion

This study found that interactions between cervical IV-RoMmax and laxity parameters were present during flexion in both neck pain patients and non-neck pain controls. Some associations were common to both patients and controls, but relationships unique to the patient group at baseline were observed. These associations in the patient group were not present at follow up, suggesting that the SMT intervention may have influenced the biomechanical behaviour of the cervical spine.

Examples of inter-motion segment IV-RoMmax and laxity correlations were demonstrated in both control and patient groups, with specific relationships, for example IV-RoMmax of (C2-C3 and C3-C4) and (C4-C5 and C5-C6) apparent in both groups at baseline and follow-up (Table 2). These results may be representative of normal intra-motion segment co-dependency, as correlations are apparent irrespective of the presence or absence of cervical pain. These findings support the notion that inter-segmental dependency exists in the cervical spine, evidence for which has already been demonstrated during sagittal bending in the lumbar spine in healthy participants⁽²⁰⁾. However, the lumbar study did not include lumbar pain participants, so it was not possible to determine whether such correlations also exist in such groups.

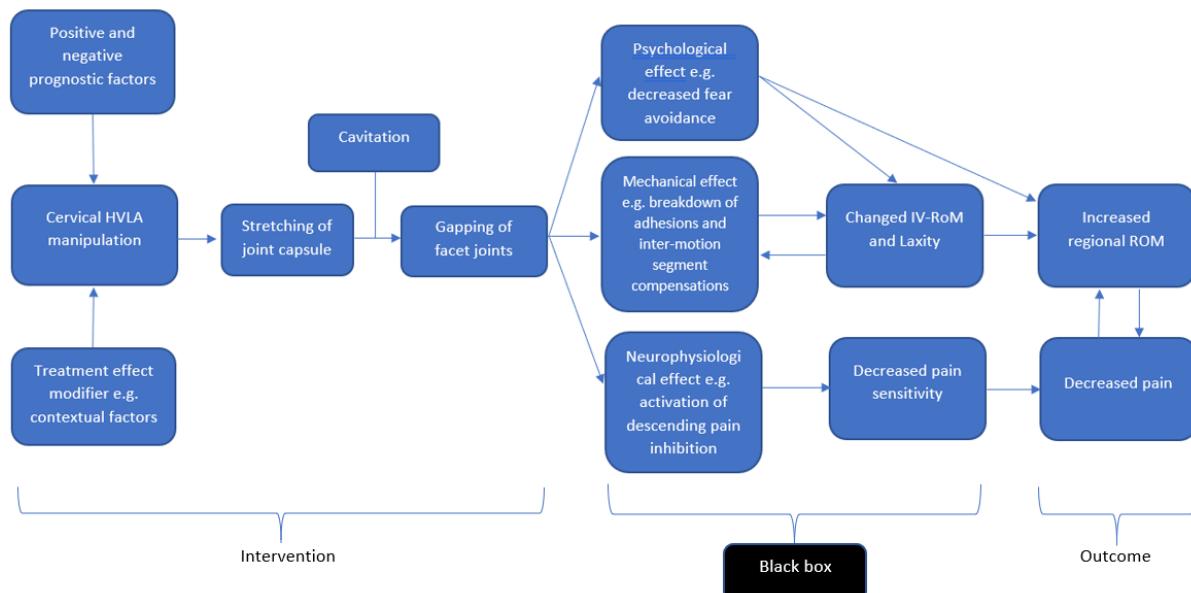
In the current study specific relationships namely, the negative association found between (C1-C2 and C5-C6) (Figure 2C) appears to be unique to the patient group at baseline. This relationship may represent a kinematic behaviour that exists only in the neck pain group as a possible strategy to achieve the required global ROM in order to compensate for changes in normal motion segment movements. There is consensus between recent studies that have investigated cervical ROM that the C5-C6 motion segment (along with C4-C5) has the largest maximal range within the cervical spine^(23, 24). It is postulated therefore that this segment might take on more relative movement to compensate for restrictions elsewhere. As the negative relationship was no longer apparent at follow-up (Figure 2D), it is suggestive that the co-dependency between these segments may have been associated (either as a cause or a consequence) with patients' pain. Indeed, patient-reported outcomes in this neck pain group, reported elsewhere⁽¹⁷⁾ demonstrated significant improvements for most participants and so the changes observed in regional kinematic behaviour may feasibly be related to the improved patient outcomes. It may have been expected then, that significant differences would be observed between the IV-RoMmax of C1-C2 and C5-C6 in patients at baseline and follow up. While there was a trend for the IV-RoMmax of C1-C2 to decrease while C5-C6 increased in range at follow-up, changes did not reach statistical significance (Table 1). It is possible that changes went undetected at levels that were not possible to measure namely C0-C1, C6-C7 and the upper thoracic spine.

Whilst there is a paucity of evidence to support a mechanism of action occurring specifically at the segmental level^(25, 26), a number of studies support the contention that interventions such as SMT and mobilisation are effective at increasing ROM⁽¹⁰⁻¹³⁾ and reducing joint stiffness⁽²⁷⁾ at the regional level. Whilst the mechanisms by which these interventions act on a patient are still largely unknown, it is proposed that a 'mechanical stimulus' may set off a sequence of neurophysiological responses that culminate in the change in clinical outcome⁽⁸⁾. This study's findings would suggest that co-dependency between the ROM of cervical motion segments may have a role to play in regional kinematic function, and therefore in clinical outcomes. The multi-segmental nature of the active structures within the neck would suggest that treatment effects involving the cervical musculature are likely of importance.

Whilst not the focus of this study, it is important to consider possible psychological mechanisms that may be acting in isolation or in tandem with the mechanical/neurophysiological effects described.

Fear avoidance for example has been shown to act as both a treatment modifier and mediator⁽²⁸⁾, and patient expectation has also been associated with management outcomes⁽²⁹⁾. Indeed, contextual factors are believed to have an important effect on treatment outcomes, the same if not more so than the manual therapy itself⁽³⁰⁾. Mechanical, neurophysiological and psychological mechanisms may all therefore contribute to the kinematic outcomes demonstrated in this study. Figure 4 provides a plausible mechanistic chain that incorporates these ideas.

Figure 4: A suggested mechanistic chain to explain the clinical effects of SMT incorporating the apparent co-dependency between motion segments (adapted with permission from Branney 2014)



The 'Black box' represents the unknown mechanisms that account for an outcome post intervention (Howick et al. 2010). In the above black box are mechanical, neurophysiological and psychological effects that may be considered to act in isolation or in concert to produce the clinical outcome. Inter-motion segment interactions/co-dependency represents an additional element, that may now be incorporated when considering such mechanisms.

The IV-RoMmax at both C1-C2 and C5-C6 in the patient group at baseline are not significantly different to those shown in controls, or indeed in the patient group at follow up. However, there is a trend observed in that C1-C2 IV-RoMmax is reduced at follow up, and C5-C6 IVRoMmax is increased. Therefore, the association change observed between the patient group at baseline and follow up (i.e. between C1-C2 and C5-C6), may possibly be an adaptation to stiffness or muscle guarding at the top of the spine.

Alternatively, movements of the neck may be considered to consist of 2 primary motions, nodding (movement occurring C0-C2) and bending (movement occurring C2-C7)⁽³¹⁾. As the relationships observed remain relatively consistent throughout the mid-cervical region, compensations are likely to take place at the very top or bottom of the cervical spine. The fact that anti-directional movements are commonplace in the region⁽³²⁾, may also explain why IV-RoMmax does not appear to mirror the inter-motion segment associations observed. The apparent co-dependency between motion segments relatively distal to each other may be explained by the synergistic behaviour of the inter-vertebral levels separating the levels, that appears to be uniform in both neck pain and non-neck pain groups. As the relationships between mid-cervical segments remain unchanged, the

lower cervicals e.g. C4-C5 and C5-C6 may be well suited to adapt to take on more ROM as motion segments previously recorded as proportionally taking on the most ROM during sagittal bending^(24, 33). This inter-segmental dependency may also be independent of morphology, as studies suggest that no difference exists between the cervical lordosis of neck pain and asymptomatic controls⁽³⁴⁾.

The results also suggest that laxity and IVRoMmax may also be co-dependents. Tables 1 and 2 demonstrate that in both the control and patient groups at baseline, when both IV-RoMmax and laxity increase at C2-C3 there is a corresponding increase at C3-C4. Likewise, in the patient group at baseline there is negative relationship between laxity at C1-C2 and C5-C6, both mirroring the findings of the IV-RoMmax parameter. Other examples of an apparent interaction between the 2 variables are shown between (C2-C3 and C4-C5) and (C4-C5 and C5-C6) in the control group, and support the notion that inter-vertebral segments that move fastest, also move furthest. It is intuitive that any absence of pre-existing relationships in the patient group at follow up, may be a result of the intervention. As such laxity should also be considered a component (i.e. an element of the black box) of the mechanisms that account for outcome post intervention (Figure 5).

Previous studies have suggested that the specificity of spinal SMT is poor⁽³⁵⁾, however this does not appear to affect outcomes^(36, 37). Whilst it is not possible to say what mechanisms of action resulted in improved patient outcomes, the findings of this study would suggest that SMT should not be thought to act solely at specific segmental levels. This agrees with the findings of a randomised controlled trial that compared the effects of cervical SMT applied to a group where the segmental level was determined by end-play motion palpation assessment, to that of a group with randomly assigned segmental level⁽³⁸⁾. The results of the Hass study showed that whilst both groups demonstrated clinically important improvements in neck pain and stiffness, there was no significant difference between groups for either outcome. This study's findings therefore support an argument that the mechanisms of action of SMT may not be segment specific, but more likely has a more generalised mechanism of action. If this is the case then neurophysiological and psychological mechanisms may be more viable than local mechanical effects. Whilst mechanical effects cannot be excluded, the findings would suggest that regionally acting structures (e.g. cervical musculature spanning multiple cervical segments) are most likely influencing the observed changes. Indeed, it might be speculated that positive treatment outcomes after SMT may be due in part to the restoration of an individual's normal (or at least more functionally optimal) regional cervical kinematic movements, and that compensatory mechanisms may extend beyond changes in adjacent segments. Future studies could explore this possibility, as mechanisms of action appear to be more complex than only affecting segments directly above or below, as segments appear to act in pairs, and interact with motion segments in different spinal regions. This is reflected in guidelines and studies that recommend the inclusion of thoracic spine SMT as being beneficial in the management of cervical pain⁽³⁹⁻⁴¹⁾. Also, as a likely globally acting mechanism, the findings may also provide an insight as to why cervical manipulation is not significantly more effective than mobilisation in the treatment of neck pain⁽⁴²⁾.

Limitations and Future Research

The use of QF in this study was limited to imaging to a single plane. The sagittal plane was selected as it is least affected by the other planes, but there remains the possibility of large movements being undetected. Whilst standardisation in this study was rigorous, it should be acknowledged that alterations in the kinematics demonstrated between baseline and follow-up in the patient group may not be solely due to the intervention. It was not ethical in this study to investigate a true control

group (ie, a neck pain population that did not receive the intervention), and so it is not known what changes may have occurred through natural history.

Further study is warranted to determine if observed kinematic changes are associated with therapeutic effects in patients with neck pain receiving spinal manipulative therapy. Whilst the idea of locally delivered SMT affecting the kinematic behaviours of distal regions is not new, this is the first study to provide evidence of co-dependence between cervical motion segments during sagittal flexion and factors that discriminate patients from controls. These findings warrant further investigation to examine possible replication in larger populations.

Conclusion

Distinct relationships were found between both intra-regional IV-RoM and laxity, many of which were present in both groups at baseline and follow up, suggestive of 'normal' kinematic behaviours. Changes in correlations unique to the patient group, may be indicative of a change in regional kinematics resulting from the manipulation intervention. Spinal manipulative therapy may have a therapeutic effect by influencing cervical kinematics at the regional level. Investigating changes in the apparent co-dependence of cervical motion segments offers a novel way of looking at spinal function. This small observational study has indicated possible differences between the kinematic behaviour of the cervical spine in patients with neck pain compared to those who are pain-free.

References

1. Bussieres A, Stewart G, Al-Zoubi F, Decina P, Descarreaux M, Hayden J, et al. The Treatment of Neck Pain-Associated Disorders and Whiplash-Associated Disorders: A Clinical Practice Guideline. *Journal of Manipulative and Physiological Therapeutics*. 2016;39(8):523-64.
2. Côté P, Wong J, Sutton D, Shearer H, Mior S, Randhawa K, et al. Management of neck pain and associated disorders: A clinical practice guideline from the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. *Eur Spine J* 2016;25 (7):2000-22. doi: 10.1007/s00586-016-4467-7.
3. Beliveau P, Wong J, Sutton D, Simon N, Bussieres A, Mior S, et al. The chiropractic profession: a scoping review of utilization rates, reasons for seeking care, patient profiles, and care provided. *Chiropractic and Manual Therapies*. 2017;25(35). doi: 10.1186/s12998-017-0165-8
4. Jun P, Page I, Vette A, Kawchuck G. Potential mechanisms for lumbar spinal stiffness change following spinal manipulative therapy: a scoping review. *Chiropractic and Manual Therapies*. 2020;28(15). doi: 10.1186/s12998-020-00304-x.
5. Peterson DH, Bergmann TF. Chiropractic technique: principles and procedures. Second ed. St Louis, Missouri: Mosby Inc; 2002.
6. Zusman M. Spinal Manipulative Therapy: Review of some proposed mechanisms, and a new hypothesis. *The Australian Journal of Physiotherapy*. 1986;32(2):89-99.
7. Maigne J-Y, Vautravers P. Mechanism of action of spinal manipulative therapy. *Joint Bone Spine*. 2003;70:336-41.
8. Bialosky JE, Bishop MD, Price DD, Robinson ME, George SZ. The mechanisms of manual therapy in the treatment of musculoskeletal pain: A comprehensive model. *Manual Therapy*. 2009;14:531-8.
9. Sterling M, Jull G, Vicenzino B, Kenardy J, Darnell R. Physical and psychological factors predict outcome following whiplash injury. *Pain*. 2005;114:141-8.
10. Cassidy JD, Lopes AA, Yong-Hing K. The immediate effect of manipulation versus mobilisation on pain and range of motion in the cervical spine: a randomised controlled trial. *Journal of Manipulative & Physiological Therapeutics*. 1992;15(9):570-5.
11. Martinez-Segura R, Fernandez-de-las-Penas C, Ruiz-Saez, M, Lopez-Jimenez C, Rodriguez-Blanco C. Immediate effects of neck pain and active range of motion after a single cervical high-velocity low-amplitude manipulation in subjects presenting with mechanical neck pain: A randomised controlled trial. *Journal of Manipulative & Physiological Therapeutics*. 2006;29(7):511-7.
12. Nilsson N, Christensen HW, Hartvigsen J. Lasting changes in passive range of motion after spinal manipulation: a randomised, blind, controlled trial. *J Manipulative Physiol Ther*. 1996;19(3):165-8.
13. Hemmila HM. Bone setting for prolonged Neck Pain: A randomized clinical trial. *Journal of Manipulative & Physiological Therapeutics*. 2005;28(7):508-15.

14. Malmstrom E, Karlberg, M, Melander A, Magnusson, M. Zebris versus Myrin: A Comparative Study Between a Three-Dimensional Ultrasound Movement Analysis and an Inclinometer/Compass Method. *Spine*. 2003;28(21):E433-E40.
15. Demaille-Wlodyka S, Chiquet C, Lavaste JF, Skalli, W, Revel M, Poiradeau S. Cervical Range of Motion and Cephalic Kinesthesia: Ultrasonographic analysis by age and sex. *Spine*. 2007;32(8):E254-E61.
16. Mieritz RM, Bronfort G, Kawchuk G, Breen A, Hartvigsen J. Reliability and Measurement Error of 3-Dimensional Regional Lumbar Motion Measures: A Systematic Review. *Journal of Manipulative and Physiological Therapeutics*. 2012;35(8):645-56.
17. Branney J, Breen AC. Does inter-vertebral range of motion increase after spinal manipulation? A prospective cohort study. *Chiropractic & Manual Therapies*. 2014;22:24.
18. van Mameren H, Drukker J, Sances H, Beursgens J. Cervical spine motion in the sagittal plane (1): range of motion of actually performed movements, an x-ray cinematographic study. *European Journal of Morphology*. 1990;28(1):47-68.
19. Breen AC, Dupac M, Osborne N. Attainment rate as a surrogate indicator of the intervertebral neutral zone length in lateral bending: An in vitro proof of concept study. *Chiropractic & Manual Therapies*. 2015;23:28. doi: 10.1186/s12998-015-0073-8.
20. du Rose A, Breen A. Relationships between lumbar inter-vertebral motion and lordosis in healthy adult males: a cross sectional cohort study. *BMC Musculoskeletal Disorders*. 2016;17(121).
21. Frobin W, Leivseth G, Biggemann M, Brinckmann P. Sagittal plane segmental motion of the cervical spine. A new precision measurement protocol and normal motion data of healthy adults. *Clinical Biomechanics*. 2002;17:21-31.
22. Schober P, Boer C, Schwarte L. Correlation Coefficients: Appropriate Use and Interpretation. *Anesthesia & Analgesia*. 2018; 126(5): 1763-1768.
23. Anderst WJ, Donaldson WF, Lee JY, Kang JD. Cervical Motion Segment Percent Contributions to Flexion-Extension During Continuous Functional Movement in Control Subjects and Arthrodesis Patients. *Spine*. 2013;38(9):E533-E9.
24. Zhou C, Wang H, Tsai T, Yu Y, Ostergaard P, Li G, et al. Intervertebral range of motion characteristics of normal cervical spinal segments (C0-T1) during in vivo neck motions. *Journal of Biomechanics* 2020;98.
25. Evans DW. Mechanisms and effects of spinal high-velocity, low-amplitude thrust manipulation: previous theories. *Journal of Manipulative and Physiological Therapeutics*. 2002;25:251-62.
26. Branney J. An observational study of changes in cervical inter-vertebral motion and the relationship with patient-reported outcomes in patients undergoing spinal manipulative therapy for neck pain. Bournemouth: Bournemouth University; 2014.
27. Shum GL, Tsung BY, Lee RY. The Immediate Effect of Posteroanterior Mobilization on Reducing Back Pain and the Stiffness of the Lumbar Spine. *Archives of Physical Medicine and Rehabilitation*. 2013;94(4):673-9.

28. Hill JC, Fritz JM. Psychosocial Influences on Low Back Pain, Disability, and Response to Treatment. *Physical Therapy*. 2011;91(5):712-21.
29. Bishop MD, Mintken P, Bialosky JE, Cleland JA. Patient Expectations of Benefit From Interventions for Neck Pain and Resulting Influence on Outcomes. *Journal of Orthopaedic & Sports Physical Therapy*. 2013;43(7):457-65.
30. Rossettini G, Camerone E, Carlino E, Benedetti F, Testa M. Context matters: the psychoneurobiological determinants of placebo, nocebo and context-related effects in physiotherapy. *Archives of Physiotherapy*. 2020;10(11). doi: 10.1186/s40945-020-00082-y.
31. Breen A. Back pain research: Skirting around the edges. *Atlas of Science*. 2018.
32. Wang X, Lindstroem R, Plocharski M, Ostergaard L, Graven Nielsen T. Cervical flexion and extension includes anti-directional cervical joint motion in healthy adults. *The Spine Journal*. 2017;18:147-54.
33. Anderst WJ, Donaldson WF, Lee JY, Kang JD. Continuous cervical spine kinematics during in vivo dynamic flexion-extension. *The Spine Journal*. 2014;14(7):1221-7.
34. Grob D, Frauenfelder H, Mannion AF. The association between cervical spine curvature and neck pain. *European Spine Journal*. 2007;16:669-78.
35. Ross JK, Bereznick DE, McGill SM. Determining cavitation location during lumbar and thoracic spinal manipulation. Is spinal manipulation accurate and specific? *Spine*. 2004;29(13):1452-7.
36. Gorrell L, Engel R, Brown B, Lystad R. The reporting of adverse events following spinal manipulation in randomized clinical trials-a systematic review. *Spine J*. 2016;16(9):1143-51. doi: 10.1016/j.spinee.2016.05.018.
37. Walker BF, Hebert JJ, Stomski NJ, Clarke BR, Bowden RS, Losco B, et al. Outcomes of Usual Chiropractic. The OUCH Randomized Controlled Trial of Adverse Events. *Spine*. 2013;38(20):1723-9.
38. Hass M, Group E, Panzer D, Partna L, Lumsden S, Aickin M. Efficacy of cervical endplay assessment as an indicator for spinal manipulation. *Spine (Phila Pa 1976)*. 2003;28(11):1091-6.
39. Blanpied P, Gross A, Elliott J, Devaney L, Clewley D, Walton D, et al. Neck Pain: Revision 2017 Clinical Practice Guidelines Linked to the International Classification of Functioning, Disability and Health From the Orthopaedic Section of the American Physical Therapy Association. *J Orthop Sports Phys Ther*. 2017;47(7). doi: 10.2519/jospt.2017.0302.
40. Martinez-Segura R, De-La-Llave-Rincon AI, Ortega-Santiago R, Cleland JA, Fernandez-De-las-Penas C. Immediate changes in widespread pressure pain sensitivity, neck pain, and cervical range of motion after cervical or thoracic thrust manipulation in patients with bilateral chronic mechanical neck pain: A randomized clinical trial. *Journal of Orthopaedic & Sports Physical Therapy*. 2012;42(9):806-14.
41. Saavedra-Hernandez M, Arroyo-Morales M, Cantarero-Villanueva I, Fernandez-Lao C, Castro-Sanchez AM, Puentedura EJ, et al. Short-term effects of spinal thrust joint manipulation in patients with chronic neck pain: a randomized clinical trial. *Clinical Rehabilitation*. 2012;27(6):504-12. doi: 10.1177/0269215512464501.

42. Leaver AM, Maher CG, Herbert RD, Latimer J, McAuley JH, Jull G, et al. A Randomized Controlled Trial Comparing Manipulation with Mobilization for Recent Onset Neck Pain. Archives of Physical Medicine and Rehabilitation. 2010;1313-8.

HERE IS WHERE THE FIGURE CAPTIONS ARE SUPPOSED TO GO

HERE IS WHERE THE TABLES AND TABLE CAPTIONS ARE SUPPOSED TO GO