The effect of manual and instrument applied cervical spine manipulation on mechanical neck pain

A thesis presented in candidature for the degree of Master of Research

By

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Abstract

This thesis investigated the effect of two different cervical manipulation techniques on mechanical neck pain (MNP) in adults. Results from studies investigating manually applied manipulation (MAM) and instrument applied manipulation (IAM) are often grouped together, with no clear indication from clinical practice guidelines if there is benefit of using one over the other. Sixty-five participants with MNP, between the ages of 18 and 35 years, were randomly allocated to one of three groups. Group 1: standardised active stretching (S); Group 2: 'S' plus a single MAM applied to the cervical spine; and Group 3: 'S' plus a single IAM applied to the cervical spine. Results indicate that MAM decreases subjective pain levels immediately and at 7 days while IAM does not. This suggests that the two techniques affect pain levels differently. Future research investigating the possibility of a threshold of force required to elicit beneficial changes and exploring other biomechanical factors such as pre-load force, acceleration and thrust amplitude will improve the efficiency of cervical manipulation.

Candidate Statement

I certify that the work incorporated in this thesis has not been submitted for a higher degree to any other university or institution.

I certify that the work presented in this thesis is my own except as acknowledged in the text.

Ethics committee approval has been obtained from the Macquarie University Human Resources Ethics Committee (Approval number: 520-140-028-1) (see Appendix A).

Signature ..... Date 25/11/14

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Finally, to my family and friends – simply, thank you. Your patience, understanding, compassion and support were invaluable. Now there is time for more fun, beach, training, racing, socialising and laughter.

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List of Abbreviations

ACTRN – Australian and New Zealand Clinical Trials Registry

CDC – Clinically detectable change

cm – centimeter

CONSORT – Consolidated Standards for Reporting of Trials

HVLA – High-velocity, low-amplitude

IAM – Instrument applied manipulation

kg – kilogram

LG – Lindsay Gorrell (research student)

LVLA – Low-velocity, low-amplitude

MAM – Manually applied manipulation

MCID – Minimal clinically important difference

mm(hg) – millimeters (of mercury)

MNP – Mechanical neck pain

MUHREC – Macquarie University Human Research Ethics Committee

N - Newtons

NDI – Neck disability index

PPT – Pressure pain threshold

RCT – Randomised controlled trial

ROM – Range of motion

Rx - Treatment

S – Stretching

sec – seconds

SF-($36v_2$) – short form questionnaire (version two)

UCLA – University of California, Los Angeles

VAS – Visual analogue scale

VBA – Vertebro-basilar artery

1. Introduction

1.1. Background

Evidence for the efficacy of spinal manipulation as a treatment for a range of musculoskeletal conditions is increasing (1-4). Spinal manipulation is commonly used to treat neck pain, a condition that has a high burden of disease globally (1, 4). The term spinal manipulation refers to a range of treatment approaches, with no clear evidence for the superiority of one technique over another (5-8). While high-velocity, low-amplitude (HVLA) spinal manipulation is commonly used in clinical practice (4, 9), this type of manipulation can be delivered in two forms: manually applied manipulation (MAM) or instrument applied manipulation (IAM) (4, 10). While there is some evidence for the efficacy of MAM, the efficacy of IAM remains unclear (4, 11, 12).

Providing evidence-based health care improves patient outcomes (13). While the results from randomised controlled trials (RCT) may not immediately translate into clinical practice, they are considered the most appropriate way to test for clinical efficacy of an intervention (3, 14, 15). Combining the results from RCTs with clinical experience underpins evidence-based healthcare (3, 16).

This thesis will report on an RCT to investigate the relative efficacy of MAM and IAM for treating mechanical neck pain (MNP).

1.2. Epidemiology of mechanical neck pain

Disability associated with neck pain has increased over the past 20 years and is currently ranked 21st in disability-adjusted life year disorders globally (17, 18). It is responsible for an increasing impact on individuals, communities, health care systems and businesses both directly and indirectly (9, 17, 19-22). Estimates of the annual costs associated with neck pain range from $US686 million in the Netherlands to $US8 billion in the United States (22, 23). As the clinical course of neck pain is episodic with variable recovery between episodes, managing the condition is important for improving quality of life for sufferers and decreasing the burden of the disorder on the wider community (2, 19, 24). The annual prevalence of neck pain is estimated to range from 30% to 50% with reports of lifetime and point prevalence values approaching those of low back pain and it is ranked 4th in years lived with disability globally (17, 18, 23-26). Women report more neck pain than men with prevalence

peaking in middle-age (35-49 years) (22, 25, 26). Non-modifiable risk factors for neck pain include age, gender and genetics while modifiable factors include social and workplace habits such as smoking, physical activity participation, sedentary work position and repetitive movements (20, 26, 27).

The Bone and Joint Decade Task Force categorised neck pain into 4 grades (27):

1) Grade I – neck pain with no signs or symptoms suggesting major structural pathology (e.g. fracture, vertebral dislocation, neoplasm) and no/minor interference with activities of daily living.
2) Grade II – no signs or symptoms of major structural pathology, but major interference with activities of daily living.
3) Grade III – no signs or symptoms of major structural pathology, but presence of neurologic deficit (*i.e.* decreased deep tendon reflexes, weakness or sensory deficit).
4) Grade IV – signs or symptoms of major structural pathology.

Mechanical neck pain (MNP) has been defined as pain in the cervical or occipital regions not associated with an identified pathological cause (1, 3, 27). This definition aligns with Grades I and II above. Figure 1 shows the distribution of neck pain as described by Guzman *et al* (shaded) and the area of MNP referred to in this clinical trial (boxes) (19). The diagnosis of MNP is based on medical history and physical examination (2, 28-30). Imaging is indicated only in the presence of a 'red flag' or with a positive finding on neurological examination (2, 27, 28). The term 'non-specific neck pain' is considered synonymous with MNP (19). As the literature is heterogeneous with respect to the epidemiology of MNP it is difficult to provide an accurate estimate of the percentage of neck pain which is specifically due to mechanical causes (22).

1.3. Spinal manipulative therapy

Manual therapy includes both thrust and non-thrust procedures (see Figure 2) (6, 31). Joint manipulation is a mechanical event in which a magnitude of force is exerted in a controlled direction to a target site, typically the spine (32). Descriptions of spinal manipulation include its effect on the nervous system (6, 32, 33). Both cervical mobilisation and manipulation have been used to manage MNP (2, 4, 9, 21). Current evidence (level B) suggests that both

approaches provide a similar effect on pain and function (3, 4, 34). Furthermore, clinical practice guidelines recommend the use of cervical spine manipulation and mobilisation for the treatment of neck pain (2, 35, 36). What is not clear in these guidelines is the nature of the spinal manipulation being recommended (10, 32, 37-39). The most common type of spinal manipulation is MAM, a manual procedure involving a thrust intended to move a joint past its physiological range of motion (ROM) without exceeding the anatomical limit (6, 33). The second type of spinal manipulation is IAM, an instrument procedure that uses mechanical instruments to affect a manipulative thrust (40).

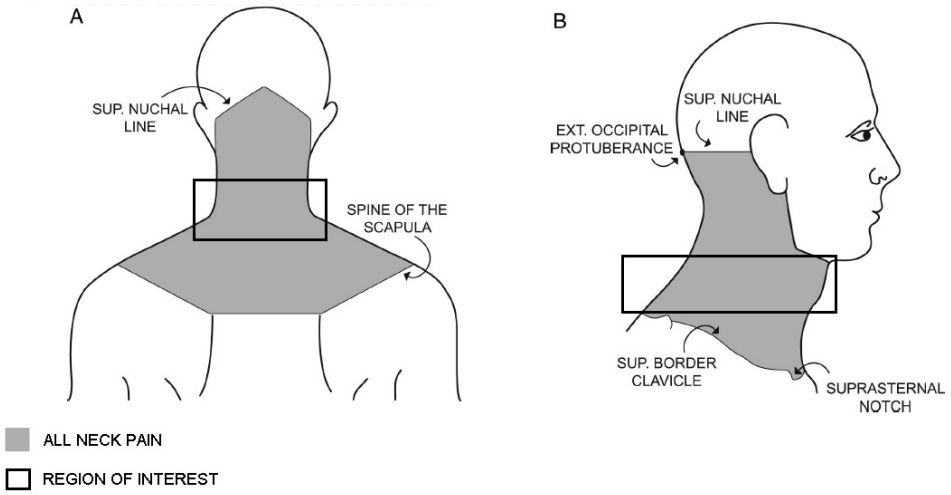


Figure 1 – The anatomic region of the neck posteriorly (A) and laterally (B) from The Bone and Joint Decade 2000-2010 Task Force on Neck Pain and its Associated Disorders adapted from Guzman et al, 2008

1.4. Force as a measure of manipulation dose

With respect to manual therapy, the term 'dose' incorporates a number of elements: magnitude of force, velocity of force delivery, amplitude of thrust, number of applications of the force, duration of the treatment and number of treatment sessions (41). For the purposes of this study, 'peak force' is used to represent the maximum force applied during the thrust phase of manipulation *i.e.* the magnitude of force.

A recent systematic review by Downie *et al*, 2010 reported peak forces exerted on the cervical spine during MAM and IAM as being approximately 100 Newtons and 40 Newtons respectively (39). Using these values as reflective of the two interventions used in this trial, MAM would be considered high force and IAM low force. During cervical MAM, the

manipulative thrust is typically delivered within 150-200ms whereas in IAM it is delivered in a shorter time, 0.1-32ms (39, 42-46). The optimal threshold of force during spinal manipulation is currently unknown as forces vary among therapists (47-49). Attributing a clinical outcome to a particular dose or technique is currently at best the result of causal association (39, 50, 51). Notwithstanding this, there is an expanding body of literature discussing the biomechanical and neurophysiological effects of spinal manipulation (32, 47, 52-54).

The amplitude and direction of a manipulative force may vary as they are controlled by the therapist who adapts to changing clinical considerations. External factors such as therapist training, experience and patient morphology have been found to directly influence the delivery of MAM (32, 50, 55). Despite the ability to control the magnitude and duration of the force, significant inter-operator inconsistencies such as variation in the application of the instrument have been reported during delivery of IAM (50, 56). Heterogeneous results between instruments used to deliver IAM have also been reported highlighting the potential for inconsistency when attempting to assess peak force or dose (50).

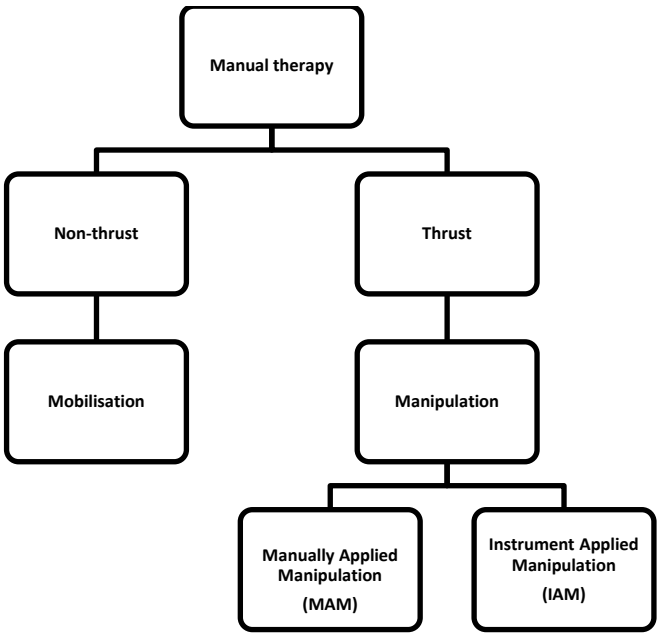


Figure 2 - Classification of manual therapy adapted from Bergman, 2011

In addition to magnitude of force, velocity of the applied force may affect the neurophysiological responses elicited by spinal manipulation (50, 57). The role of manipulative pre-load forces in eliciting positive changes have also been reported (32, 47,

48, 56). In IAM pre-load forces may vary (50, 56) with reports these forces may not be sufficient to elicit positive changes (47). Furthermore, it has been proposed that the effects of transmitted loads (applicable with IAM) may be different to applied loads (MAM) due to the effects of patient pre-positioning and the active and passive properties of the intervening tissues (33). As an example of this, increased muscle tension may absorb and thus diminish a percentage of the applied force reaching the mechanoreceptors. In addition to this, co-activation may contribute to the complex neurophysiological response of the nervous system to joint manipulation (58). Co-activation involves the accumulation of signals received from cutaneous receptors, muscle spindles, Golgi tendon organs and mechanoreceptors embedded in the joint capsule, in turn eliciting a neurophysiological response. It has been reported that the threshold of dose (peak applied force) required to elicit a co-activation response following chiropractic manipulation is 40 Newtons (N) (59). As MAM and IAM apply approximately 100 and 40 N respectively (39), it is possible that both may elicit co-activation. . Reflex responses subsequent to MAM are reported to excite a relatively large pool of motor neurons both at and adjacent to the involved segment while stimulation from IAM appears to be restricted to the area of application (32).

Vertebral movement resulting from MAM has been reported as less than 10mm of linear displacement in the lumbar spine (33, 60) while for IAM movements ranging from 0.15 to 0.66mm (medial-lateral), 0.15 to 0.81mm (posterior-anterior) and 0.07 to 0.45mm (axial) have been reported for patients undergoing lumbar decompressive surgery (61). Although the extent of linear displacement in the cervical spine has not been established, it is reasonable to expect it to be less than that for the lumbar spine as the forces exerted during cervical manipulation are significantly less than for manipulation of the lumbar spine (39).

Pentelka *et al* investigated the effect of repetition and duration of lumbar spine mobilisation on pressure pain thresholds (PPT). They reported the greatest hypoalgesic effects occurred with at least four sets of mobilisations and were independent of the duration of the mobilisation (30sec *versus* 60sec) (41).

1.5. Trial rationale

Aim: the aim of this research was to investigate the relative effects of two different cervical spine manipulation techniques in adults with MNP.

Research question: the research question addressed by the trial was: 'Is there a difference in efficacy between MAM and IAM cervical spine manipulation?'

Null Hypothesis (H_0): there is no difference in efficacy between MAM and IAM cervical spine manipulation.

1.6. Summary

This chapter introduced the reader to the topic, provided the aim, research questions, and rationale for why it is important to conduct this research. The following chapter is a review of the literature discussing cervical spine manipulation for the treatment of MNP.

2. Literature Review

2.1. Neurophysiological effects of spinal manipulation

Much of the literature discussing neurophysiological effects of spinal manipulation refers to the lumbar spine (54, 62). However, some extrapolation of these findings to the cervical spine is possible as both regions have some common anatomical and physiological attributes.

Neurophysiological influences:

In spinal manipulation, a biomechanical stimulus initiates neurophysiological responses such as hypoalgesia. This effect may be dependent on both the force and force/time profile of the manipulation (49). Motion of a vertebral segment produces transient biomechanical effects rather than lasting positional change (63, 64), and as there are significant variations in the mode of delivery of manipulation due to inter and intra-practitioner variation it is possible that additional mechanisms such as central and peripherally mediated processes may be involved in producing an hypoalgesic effect (53, 65). Complex interactions between the peripheral and central nervous systems characterise the pain experience and make it difficult to identify the exact mechanism(s) associated with the interaction. However, it is hypothesised that there is a link between hypoalgesia and the activity of the sympathetic nervous system following spinal manipulation which may be mediated by both the periaqueductal gray and dorsal horn of the spinal cord (62).

Centrally mediated mechanism:

An indirect spinal cord mediated response following spinal manipulation may induce hypoalgesia (66, 67), afferent discharge (68, 69) and changes in muscle activity (70, 71). Furthermore, spinal manipulation may inhibit A-δ fibre mediated pain perception by modulating dorsal horn excitability at the respective segmental level (72, 73). A central pain control mechanism involving stimulation of descending inhibitory pain pathways and several supraspinal structures has also been proposed (74). These supraspinal structures include the anterior cingular cortex, amygdala, periaqueductal gray and rostral ventromedial medulla (75-77).

Peripherally mediated mechanism:

Peripheral musculoskeletal injuries typically elicit a local inflammatory response which

contributes to the healing process in addition to influencing pain processing. It has been proposed that inflammatory mediators and peripheral nociceptors may also be directly affected by spinal manipulation (74, 78). Studies measuring the levels of blood markers pre and post- manipulation observed changes in β-endorphin, anandamide, serotonin and endogenous cannabinoids providing some objective evidence for an hypoalgesic effect following manipulation (79-81). In addition to this, studies reporting increased PPT measured at the lateral epicondyle following cervical spine manipulation in participants with lateral epicondylalgia suggest the possibility of effects that are remote to the treatment site (82-84).

2.2. Manually applied HVLA manipulation (MAM)

There have been several reviews reporting proposed mechanisms underpinning MAM, the majority of which relate to the lumbar spine (33, 62, 69, 85). The summary presented below includes past and current theories relating to the effects of MAM. These can be grouped under four main headings:

1. Release of entrapped synovial folds or plica.
2. Relaxation of hypertonic muscle by sudden stretching.
3. Disruption of articular or periarticular adhesions.
4. Unbuckling of motion segments that have undergone disproportionate displacements (69, 86).

1. Release of entrapped synovial folds or plica

The hypothesis that entrapped synovial folds are a source of acute locked back was investigated by Bogduk and Jull. They proposed that for this to be possible, the joint must "be in, or near to, a neutral position, for only in that position are the articular surfaces sufficiently apposed to trap a meniscus (or synovial fold)"(87) . A patient with acute locked back typically presents in flexion with an inability to extend. Synovial fold entrapment is unlikely to be the cause with such a presentation as the joint would not be in a neutral position. The theory of pain secondary to distortion of the zygapophyseal joint capsule created by entrapment of fibro-adipose meniscoids was rejected on the basis that it is unlikely the meniscoids would be adequately strong to create this deformation (87-89).

A more plausible hypothesis proposed that flexion of the lumbar spine moved the inferior articular process of a zygapophyseal joint superiorly, dragging a meniscoid with it. When moving into extension, this inferior articular process returns towards its neutral position. The meniscoid fails to re-enter the joint cavity, impacting instead against the edge of the articular cartilage and buckling or entrapping it. Entrapment stimulates nociceptive receptors located within the zygapophyseal joint capsule (6, 87, 90). A similar phenomenon may occur in the cervical spine, however excessive rotation rather than extension is the likely precipitating movement with de-rotation instigating meniscoid impaction (69, 91).

2. Relaxation of hypertonic muscle by sudden stretching

The theory that MAM results in the relaxation of hypertonic muscles due to sudden stretching was refuted by Lederman. He showed that reduced motor tone seen post-manipulation resulted from the stimulation of inhibitory afferents not sudden stretching of hypertonic muscles (92). He argued that sudden stretching of the meniscus produced with this type of manipulation would excite rather than inhibit the motor neuron, increasing rather than decreasing tone within the muscle (92). Fryer argued that while there is little direct evidence supporting the theory, sustained muscle contraction is a feature of intervertebral dysfunction and the concept of protective muscle spasm remains plausible (93).

Recent studies have demonstrated reductions in paraspinal electromyographic activity and hyperalgesia of paraspinal myofascial trigger points in the cervical spine following manipulation suggesting that any observable 'motor' effects caused by MAM may be mediated by the dorsal horn (94-96).

3. Disruption of articular or periarticular adhesions

Lewit examined the cervical spine of ten patients prior to abdominal surgery and again during anaesthesia and intubation and found, without exception, that movement restrictions remained unchanged and were more easily induced when the patient was completely relaxed. He concluded that movement restriction was an articular phenomenon caused by a mechanical 'obstacle' within the joint (97). While it is theoretically possible that this 'obstacle' could be a meniscoid as described in point 1, there is some evidence to suggest that articular blockage is most likely due to the strong elastic recoil exerted by the joint itself. In this instance, elastic recoil results from interaction between atmospheric

pressure and the cohesive properties of synovial fluid which behaves like a solid when exposed to high shear rates such as those experienced during spinal manipulation (98-100). Applying MAM in this scenario would therefore at best produce a temporary increase in range of motion (69, 99).

4. Unbuckling of motion segments that have undergone disproportionate displacements

This hypothesis originated from one of the oldest theories of spinal manipulation where the sound associated with cavitation, 'crack', was considered to signify the reduction of displaced segments in the spinal column (101). This theory has been disproved by several biomechanical studies demonstrating that the involved segment undergoes transient movement rather than positional change (33, 60, 102). Cyriax suggested that spinal manipulation resulted in the 'replacement' of fragments of the nucleus pulposus (103). This theory, advocated by some as an explanation for both the sound of cavitation and any hypoalgesic effect (104) is unlikely to be accurate because if true, it does not explain cavitation in peripheral joints which do not contain intervertebral discs (69). In addition to this, cavitation of all spinal joints during a single intervention session would not be possible as it is highly unlikely that a displaced fragment of a nucleus pulposus would be present in multiple spinal joints simultaneously (69).

2.3. Instrument applied manipulation (IAM)

In this trial, an Activator® IV adjusting instrument was used (see Section 3.6.1). A review of the literature related to Activator® IAM reveals two peer-reviewed publications addressing the history and progression of the Activator® Adjusting Instrument (105, 106). It is worth noting that the lead author in both publications is the co-founder of the Activator® Methods Chiropractic Technique. The first reference to use of a 'tool' applied to the human spine delivering percussive thrusts was published in March 1935 (107). The modern Activator® is a sophisticated instrument compared to the initial tool which was based on a dental impactor (106, 108). It is able to deliver a relatively low peak force with small thrust duration compared to other spinal manipulation instruments (43). There is some evidence suggesting that certain vibratory frequencies have the ability to either promote or prevent healing (109-111).

Frequencies closely matched to the natural resonance of body tissues conduct external forces more efficiently through the body (112). This theory led researchers to investigate the

ability of IAM to induce resonant frequencies in skeletal tissue (45, 112-114). It has been proposed that more effective transmission of the manipulative force during an IAM may occur as a result of the matching of spinal resonant frequencies and that a more efficient transmission of the manipulative force is achievable in humans (105, 112) . Resonant frequencies have been quantified as 30-50Hz in the posterior to anterior plane and 3-5Hz in the inferior to superior plane (110-112). While the influence of resonant frequency force transmission across symptomatic segments is yet to be established (105), it has been proposed that any movement of bone induced by IAM may be comparable to those occurring in MAM (61, 115, 116). However, the challenge to accurately measure vertebral displacement must be met before generalised statements concerning relative differences between the two approaches can be made. In addition to this, the effect of muscle activity on spinal motion during manipulation must be considered as it is reasonable to predict that hypertonic musculature would absorb any increased levels of force, altering the amount that reaches the mechanoreceptors (117).

Cutaneous receptors, muscle spindles, Golgi tendon organs and mechanoreceptors embedded in the joint capsule all convert mechanical force into neural impulses. Accumulation of this process is known as co-activation, and may explain the complex neurophysiological response of the nervous system to spinal manipulation (58). It has been suggested that the threshold of dose (in terms of peak applied force) required to elicit a co-activation response is 40N (59). As an Activator® delivers approximately 40N of force it is possible that it may elicit co-activation. It is pertinent at this point to examine the literature discussing the differences between MAM and IAM.

2.4. Current literature

2.4.1. Efficacy of MAM *vs* IAM

There have been three studies investigating the efficacy of cervical MAM compared to IAM for the treatment of MNP (see Table 2). The studies display heterogeneous methodologies with participant numbers ranging from 14 to 47, different outcome measures and a variable number of intervention sessions (single session to multiple sessions over 4 weeks) (118-120). These studies concluded that MAM and IAM were equally beneficial.

The methodological quality of the studies was assessed using the Cochrane Back Review Group criteria. These criteria were specifically designed to evaluate trials in the field of spinal

disorders (see Table 1) (21, 121). The internal validity of the three studies was deemed 'low quality' *i.e.* to have a high risk of bias (121). In this analysis, the median score for study quality was 4.33, with a range of 4-5. None of the studies achieved a score of 6 or greater out of 13, the threshold for classification as 'high quality'. Unsatisfactory blinding of participants, practitioners and outcomes assessors, incomplete outcome data and intention-to-treat analysis were sources of methodological bias in these studies.

Performance bias occurs with non-blinding of participants and practitioners. This non-blinding may result in differences between the treatment groups separate to the intervention being investigated. In these studies, the effect of non-blinding is unknown as it is possible that participants or practitioners may have acted differently due to group allocation. Additionally, non-blinding of the outcomes assessor may result in detection bias as the beliefs of the assessor may influence how participants respond to treatment. Attrition bias occurs when there is incomplete reporting of outcome data which may result in a falsely inflated effect in one group (121, 122). Heterogeneity in trial design and reporting of outcome measures across the studies prevented meta-analysis of the data.

2.4.2. Manual therapy and dose optimisation

As mentioned in section 1.4, manual therapy dose is composed of a number of elements: force magnitude, velocity, amplitude of thrust, number of repetitions and duration of treatment (41). An increasing number of reports of dose optimisation for manual therapy are appearing in the literature with several recent publications discussing the application of a mechanical device to control inter-practitioner variability for elements such as pre-load force, force magnitude and thrust duration. Results obtained from these studies support the theory that there is a link between force and the neurophysiological response in spinal manipulation (47, 48, 56).

Dishman and Bulbulian compared the effect of spinal manipulation and mobilisation on the amplitude of the tibial nerve Hoffmann reflex in the gastrocnemius muscle of 17 non-human subjects and reported a similar magnitude in alpha motoneuron excitability between the two groups (manipulation or mobilisation). Based on these results, they proposed that neither force magnitude nor velocity of the thrust were of great significance when considering the reflexive inhibition of the motor neuron pool *i.e.* the neurophysiological response to spinal manipulation (123).

More recently, other studies have suggested that a force threshold must be reached to induce hypoalgesia in participants with lateral epicondylalgia and chronic, non-specific neck pain (49, 124). McLean *et al* subjected six participants to four different magnitudes of spinal manipulation: 33%, 50%, 66% and 100% of maximum force and reported that the level of force was critical in eliciting an hypoalgesic effect (124). In support of this, Snodgrass *et al* reported that participants in the high force group (90N) had less pain than those in the lower force group (30N) and less stiffness than the placebo group (49). Both studies recommended further research to investigate dose optimisation in manual therapy.

Table 1 – Assessment of methodological bias in current literature investigating MAM vs IAM for the treatment of MNP (118-120)

Study	*Random sequence generation (selection bias)*	*Allocation concealment (selection bias)*	*Blinding of participants*	*Blinding of personnel/care givers (performance bias)*	*Blinding of outcome assessor (detection bias)*	*Incomplete outcome data (attrition bias)*	*Selective reporting (reporting bias)*	*Group similarity at baseline (selection bias)*	*Co-interventions (performance bias)*	*Compliance (performance bias)*	*Intention-to-treat-analysis*	*Timing of outcome assessments (detection bias)*	*Other bias*	Total
Yurkiw 1996	+	-	-	-	+	?	+	?	+	NA	?	+	?	5
Wood 2001	?	?	-	?	?	?	+	+	+	?	?	+	-	4
Gemmell 2010	+	+	-	-	-	+	?	-	?	?	?	+	?	4

+ indicates item present in study; - indicates item not present in study;? indicates it is unclear if item was present in study

2.5. Remote effects of manipulation

The potential for remote effects following MAM that are facilitated by the autonomic nervous system has some support in the literature (125, 126). Early work investigating this relationship focused on investigating a historical concept known as 'subluxation'.

'Subluxation' has been described as joint dysfunction that results in fixation and/or malposition of the joint which then alters its biomechanical properties (127, 128). More

Table 2 – Current published literature investigating MAM vs IAM for the treatment of MNP

Study	***Participants***	***Interventions***	***Sessions***	***Clinical Setting***	***Outcome Measures***	***Conclusion***	***Quality Assess***
Yurkiw & Mior, 1996 **(118)**	14	Group A: Activator® Group B: HVLA cSMT	One	Yes	• LF ROM • VAS	No statistically significant differences before or after the interventions	5
Wood *et al*, 2001 **(119)**	30	Group A: Activator® II Group B: HVLA cSMT	2-3/wk for 4wk or until asymptomatic	Yes	• Numerical pain rating scale 101 • McGill SF questionnaire • NDI • Goniometer	Both instrumental & manual SMT have beneficial effects associated with reducing pain & disability and improving cROM	4
Gemmell & Miller, 2010 **(120)**	47	Group A: HVLA cSMT Group B: LVLA mob Group C: Activator® IV	2/wk for 3wk or until asymptomatic	No	• Patient global impression of change • SF-36v_2	All 3 methods had a 'long-term benefit'	4

HVLA: high-velocity, low-amplitude; cSMT: cervical spinal manipulative therapy; LF: lateral flexion; VAS: visual analogue scale; SF: short form; NDI: neck disability index; LVLA: low-velocity, low-amplitude; SF-36v_2 : short form 36 questionnaire version 2.

recently, researchers have focused on the link between the sympathetic nervous system and reflex responses following spinal manipulation and how these responses may be linked to pain perception (123, 125, 129). A recent systematic review reported that changes in skin conductance, respiratory rate, blood pressure and heart rate could occur in healthy populations following mobilisation of specific areas of the spine (130). These findings are supported by reports of parasympathetic responses following cervical spine manipulation in healthy individuals (129).

In addition to responses in the autonomic nervous system, cervical spine manipulation has been associated with changes in the somatic nervous system (131, 132). Studies investigating the effects of cervical spine manipulation on lateral epicondylalgia described both sensory and motor changes including increased hand grip-strength and hypoalgesic effects at the elbow (82, 84, 133). Other studies have demonstrated excitatory effects of spinal manipulation on motor activity (134-136). Interestingly, it has been reported that repeated sessions of cervical spine manipulation may produce a cumulative effect on grip strength suggesting the possibility of a dose-response mechanism (84).

2.6. Current clinical guidelines for mechanical neck pain

Although cervical spine manipulation is commonly used to treat MNP, techniques that include rotation and its effect on the vertebral artery remain unclear (30, 137, 138). Biomechanically, end-range movement of the cervical spine is facilitated by the upper thoracic spine. Therefore biomechanical changes elicited by treating the upper thoracic spine have the potential to produce changes in the adjacent cervical region (139, 140). Furthermore, altered thoracic joint motion may be an underlying contributor to biomechanical disorders of the cervical spine (140, 141). In support of this, neck pain has been reported to be associated with hypomobility of the upper thoracic spine (142-144). In light of this, thoracic spine manipulation has been investigated as an effective and safer alternative (2, 3, 21, 145). It is therefore biomechanically feasible that resolution of thoracic spine dysfunction may result in positive outcomes for cervical spine disorders.

2.6.1. Cervical vs thoracic manipulation & mobilisation

Studies comparing cervical and thoracic spine manipulation for the treatment of MNP have been reported in the literature (73, 146-148). Due to the heterogeneous design of these studies, it is difficult to draw definitive conclusions concerning the efficacy of the two

approaches. In general, studies that included the application of spinal manipulation to several areas of the spine reported greater reductions in disability compared to those receiving manipulation to the cervical spine alone (147, 148). Some participants responded more favourably to cervical compared to thoracic spine manipulation while others experienced similar changes regardless of the area treated (73, 146).

These results have led to a call for further studies comparing the effect of varying the location of the applied force (21, 149, 150). Furthermore, evidence suggesting that cervical manipulation and mobilisation may be equally effective in treating MNP has appeared in the literature (1-3, 5, 21, 151, 152). However, a recent Cochrane review highlighted the view that the relationship between optimal technique and dose for the treatment of MNP remains unknown (21). Studies investigating dose optimisation of thrust compared to non-thrust techniques in the treatment of MNP have been published (49, 94, 153, 154). The results of these studies suggest that thrust approaches applied to both the cervical and thoracic spines are associated with more significant short-term benefits for patients with MNP than non-thrust techniques (49, 94, 153, 154). Despite these findings, the studies displayed heterogeneity in both methodology and interventions and as such, should be interpreted with caution.

2.6.2. Multimodal approach for mechanical neck pain

A multimodal approach to treating MNP that includes ancillary procedures, regardless of whether the manual therapy was manipulation or mobilisation is supported by the literature (1-4, 19, 21, 151). The most commonly used ancillary procedure reported was exercise, specifically stretching and strengthening of cervical and scapular muscles (1, 2, 155, 156). It has been suggested that manual therapy provides an initial short-term hypoalgesic effect while exercise decreases pain and increases function over a longer period of time (11, 12, 155, 157). Improved cost-effectiveness and patient perceived recovery using a multimodal approach have also been reported (157-159). The literature highlights the need for further research to determine dose optimisation and cost-effectiveness while also advocating the use of ancillary procedures (4, 11, 155).

2.7. Risk: benefit analysis of MAM and IAM cervical spine manipulation

While cervical spine manipulation is reported to be an effective treatment for MNP (1-3), its use remains controversial due to concerns relating to the safety of the intervention (138, 160, 161). There is currently no single standard for reporting serious adverse events following spinal manipulation. Estimates of the incidence of adverse events following cervical spine manipulation range from 1 in 50,000 manipulations to 1 in 5.85 million (138, 162, 163). In reality, the true incidence remains unknown and is currently the focus of ongoing research (137, 138).

Rothwell *et al* reported that patients younger than 45 years were five times more likely to have visited a chiropractor within one week of experiencing a vertebro-basilar artery (VBA) stroke (164). Similarly, Smith *et al* found that VBA stroke patients were approximately six times more likely than controls to have received cervical spine manipulation within 30 days of their stroke (165). However, more recent studies report a temporal rather than causal association between VBA stroke and cervical spine manipulation (166). Cassidy conducted a population-based case-crossover study and concluded that there was a similar risk of VBA stroke in individuals regardless of whether they sought care from a physician or chiropractor (137). He suggested that patients seek care for the early symptoms of VBA stroke e.g. neck pain and headache, and that chiropractic care does not actually increase the risk of VBA stroke. This finding is supported by Boyle *et al* who reported that at a population level, chiropractic care was not associated with fluctuations in the incidence of VBA stroke but rather the patient may already have been exhibiting the early signs of stroke prior to receiving chiropractic intervention (167). In addition to this, there is a nascent body of literature suggesting that the forces experienced by the vertebral artery during cervical spine manipulation are significantly lower than the level of force required to mechanically disrupt the artery (46, 168, 169).

More commonly a patient will experience minor, temporary side effects from cervical spine manipulation such as headache, pain, stiffness or minor discomfort (170). This is reflected in Gross *et al's* recent Cochrane review of 27 studies investigating the use of cervical manipulation or mobilisation for neck pain (21). Of the eight studies recording adverse events, three reported no side effects while the remaining five reported only minor and

temporary effects. Serious adverse effects such as stroke or ongoing neurological deficits were not reported in any of the trials. In addition to this, it has been suggested that if contraindications and red flags were ruled out, approximately 45% of all adverse events associated with cervical spine manipulation could be prevented (138). This highlights the importance of performing a thorough medical history and physical examination in addition to incorporating sound clinical reasoning prior to administering cervical spine manipulation. This concept is supported by Rushton *et al* who acknowledged that although the likelihood of serious adverse events was low, there remained a small risk associated with the delivery of cervical spine manipulation. This risk depended on both the patient's clinical presentation and the presence of any cardiovascular risk factors such as hypertension and/or atherosclerosis (30). The responsibility therefore falls to the clinician to identify these risks. In doing so, it must be remembered that clinical decisions are made in the absence of certainty and are based on assessing risk compared to benefit (see Table 3).

Although a clinician assesses the risks and benefits before administering cervical spine manipulation, current clinical practice guidelines do not distinguish between MAM and IAM. Highlighting this point, several authors have stated the need for more trials comparing cervical spine manipulation techniques in isolation (single intervention) to allow for uncontaminated effect estimates pertaining solely to each technique (4, 171). This concept was also explored by Hurwitz *et al* who compared the relative adverse effects of cervical spine manipulation and moblisation in 280 participants enrolled in the UCLA neck pain study. In this study, there was greater reporting of adverse events associated with cervical spine manipulation compared to mobilisation. It was reported that participants who received manipulation were less satisfied with care, perceived less improvement in neck symptoms and experienced more pain and disability at 4-week follow-up (172).

Taylor *et al* reviewed the literature investigating the safety of IAM and reported that IAM was associated with no more risk than MAM (37). However, it was highlighted that the available literature on the topic was weak and that there were in fact no studies directly addressing the issue of safety for IAM (37). To the author's best knowledge, there have been no studies to date that directly evaluate the relative safety of IAM compared to MAM.

Table 3 – Decision making framework for analysing risk: benefit of cervical manipulation as per Rushton et al, 2014

Risk	Benefit	Action
High number/severe nature of risk factors	Low predicted benefit of manual therapy	Avoid treatment
Moderate number/moderate nature of risk factors	Moderate predicted benefit of manual therapy	Avoid or delay treatment/monitor & reassess
Low number/low nature of risk factors	Low/moderate/high predicted benefit of manual therapy	Treat with care/continual monitoring for change/new symptoms

2.8. Summary

The literature published on MAM and IAM reveals an evolution in both approaches over a relatively short period of time. While the use of cervical spine manipulation for the treatment of MNP remains controversial, current research suggests that if the appropriate history and physical examination are performed it is a relatively safe intervention to administer. Biomechanical studies highlight the application of both MAM and IAM in the cervical region are dependent on several factors which display inter-practitioner variability.

Many questions remain concerning the magnitude of force required for dose optimisation of spinal manipulation when used for the treatment of MNP. Although current guidelines endorse a multimodal approach, investigation of specific manipulation techniques is recommended. Adequately powered studies with sound methodological design investigating the relative efficacy of different types of spinal manipulation are required. Results from such studies could then be used to inform clinical practice guidelines. Combining best evidence and clinical experience aligns with Sackett's definition of evidence based medicine (173). In addition to the development of more robust guidelines, the validation of manual therapy as an effective and relatively safe intervention may result in an increased acceptance of its use by other health practitioners (53). The trial reported in this thesis will add to the current body of knowledge by exploring the relative efficacy of two different types of cervical spine manipulation for MNP.

3. Methodology

3.1. Clinical trial approvals

Ethics Approval

The trial was approved by Macquarie University's Human Research Ethics Committee (MUHREC) on 21st July 2014. (Approval number 520-140-028-1) (see Appendix A).

Clinical Trial Registration

This trial was registered with the Australian and New Zealand Clinical Trials Registry on 29th July 2014. (ACTRN12614000804684)(see Appendix B).

3.2. Methods

3.2.1. Setting

The trial was conducted at Macquarie University's Chiropractic Outpatient Clinic located in the EMC^2 building, 3 Innovation Rd, Macquarie University, NSW, Australia 2109.

3.2.2. Screening and consent processes

Volunteers responded in the first instance to written advertisements (see Appendix C) placed around the Macquarie University campus which directed them to contact the research student (LG) to arrange an appointment for the initial screening visit. Recruitment occurred from 6th August to 6th September 2014. Once a volunteer had satisfied the inclusion and exclusion criteria (Table 4), read the Patient Information and Consent Form (see Appendix D) and provided written consent they were enrolled as a participant in the trial. A participant was then asked to provide a full medical history and undertake a physical examination. Participants with a history of trauma to the neck were included in the study provided the event occurred more than twelve months previously and it was deemed by LG not to influence the diagnosis of mechanical neck pain. On completion of these investigations, a participant was assigned a trial specific identification number and randomly allocated to one of three groups using a computer generated random number sequence created by an administrative officer in the Department of Chiropractic who had no further involvement in the trial. The group allocation was delivered to a participant in an individual opaque envelope by LG. The three groups were: Group 1 – standardised active muscle stretching (S); Group 2 – the same active muscle stretching routine plus a single high force MAM; or Group 3 – the same active muscle stretching routine plus a single low force IAM.

Table 4: Inclusion and exclusion criteria for study participants

Inclusion Criteria	Exclusion Criteria
• Age 18 – 35 years • Mechanical neck pain originating from the lower cervical spine (C5-C7)	• Contraindication to cervical spinal manipulation • Current pregnancy • Pre-existing condition which may alter the effect of spinal manipulation (e.g. connective tissue disorders) • Cervical pain which is not of mechanical origin • Cervical pain that does not originate from the lower cervical spine (C5-C7) • Having received cervical spinal manipulation within the preceding one month • Current use of anticoagulant therapy • History of recent surgery and/or recent neck trauma (past 12 months) • Facial or intra-oral anesthesia or paresthesia • Visual disturbances and/or blurred vision and/or diplopia • Dizziness and/or vertigo • Nausea and/or tinnitus and/or drop attacks and/or dysarthria and/or dysphagia

3.2.3. Spinal manipulative practitioners and outcomes assessor

All cervical spine manipulation was administered by qualified Chiropractors experienced in either MAM or IAM. All outcome assessments including pre and post-intervention measurements in addition to the administration of the standardised stretching program were carried out by LG. All MAM was administered by Dr Roger Engel (supervisor), a registered Chiropractor with over 30 years clinical experience performing spinal manipulation. All IAM was administered by Mr Tim Wade-Ferrell, a Chiropractor with over 25 years clinical experience in the administration of spinal manipulation and an accredited Activator® practitioner.

3.2.4. Diagnostic criteria

Current clinical practice guidelines recommend the use of a number of clinical tools in addition to taking a medical history when diagnosing MNP (3, 22). These tools include a physical examination that incorporates an assessment of active cervical range of motion (ROM), cervical and thoracic segmental mobility testing, cervical flexion testing, deep neck flexor endurance testing and subjective outcome measures such as impact on activities of daily living (2). These tests were performed on each participant. Specifically, a participant was included in the trial if they reported pain in the cervical or occipital region that originated from the lower cervical spine (C5-7) with movement or prolonged static postures (27), restriction in cervical and/or thoracic ROM, exhibited a diminished capacity to perform cervical flexion and deep neck flexor endurance testing with no neurological signs, instability in the cervical region or a positive provocative pre-position test (2, 30). Furthermore, participants were asked to state to what extent they believed their neck pain influenced their activities of daily living. In this trial, the diagnosis of MNP was made by LG based on medical history (2, 3, 27) and results from the tests described above. It has been acknowledged that a diagnosis of mechanical neck pain does not have to include the cause of pain but rather what aggravates the pain (29).

3.3. Outcome measures

The trial measured several outcomes including pain, cervical ROM, grip strength and wrist blood pressure. The primary outcome measure was pain measured using a visual analogue scale (VAS), numerical pain rating scale (NPRS) and pressure pain threshold (PPT) while the secondary outcomes comprised active cervical ROM, grip strength and wrist blood pressure. With the exception of NPRS, all outcomes were measured pre and immediately post-intervention. Participants were also asked to respond to a telephone text message reporting their neck pain using the NPRS at 7 day follow-up.

Van Tulder *et al* emphasised the importance of defining the minimal clinically important difference (MCID) for each outcome measure in clinical research (174). The MCID has been defined as the smallest treatment effect or the lower boundary of change necessary to be considered clinically important (175-177) and is reportedly context-specific rather than a fixed value (175). The literature reports difficulty describing accurate MCID values for some measures due to heterogeneity in the reporting of changes *i.e*. by the clinician or patient,

and also differences in the interpretation of these changes (175, 178, 179). The value of outcome measures is dependent on high intra-rater and inter-rater reliability and refers to the ability of a measure to be sufficiently accurate when repeated by the same individual and the capacity of the measure to remain accurate when used by different individuals (180).

3.3.1. Primary outcome measures

The primary outcome assessment was change in neck pain and was evaluated using two types of measures: subjective pain (VAS and NPRS) and objective pain (PPT).

Visual analogue scale (VAS)

The VAS is a commonly used eleven-point subjective measure of pain which is a valid and reliable tool for measuring pain (181-183). The reported MCID for VAS ranges from 1.7 to 2.1 centimeters (1.7-2.1 on the scale used in this trial) (184, 185).

Numeric pain rating scale (NPRS)

The NPRS is a commonly used eleven-point scale which has been reported as performing well for describing pain intensities in the central portion of the continuum (2-8) (186, 187). The NPRS exhibits sufficient test-retest reliability, is adequately responsive when used to describe changes associated with mechanical neck pain and has a reported MCID of 1.3 points (188). The NPRS consisted of the standard question 'Out of 10 how is your neck pain today?' sent to all participants via telephone text message at 7 day follow-up.

Pressure pain thresholds (PPT)

Pressure pain thresholds were measured over the spinous process of the involved segment (C5-C7). In the absence of an exact value for MCID, increases of 25% or greater from baseline have been regarded as clinically significant for PPT (65, 189). PPT is a widely used measure of change in pain levels with a high level of both intra-rater and inter-rater reliability (180, 190-194).

3.3.2. Secondary outcome measures

Secondary outcome measures included cervical ROM, grip strength and wrist blood pressure.

1. Cervical ROM, measured using an inclinometer in this trial, is a commonly used outcome measure to assess the effectiveness of cervical spine manipulation (195). A recent systematic review questioned the predictive validity of ROM in a clinical setting and highlighted the heterogeneous nature of current clinimetric studies investigating its reliability (195). However, previous studies have reported adequate performance of inclinometers with respect to reproducibility, validity and responsiveness in patients with MNP (28, 196, 197). The clinically detectable changes (CDC) for cervical ROM testing are provided in Table 5 (198, 199).
2. Grip strength was measured using a dynamometer with clinimetric data suggesting it has good test-retest, inter-rater and intra-rater reliability (200, 201). Studies report that a change of 6kg is considered to be a CDC and therefore significant (202).
3. Wrist blood pressure was measured using a digital wrist sphygmomanometer. There are no reported MCID values for blood pressure. One study investigating the effects of antihypertensive therapy on elevated blood pressure concluded that the value for a clinically significant reduction in blood pressure was extremely variable and differed between patients (203).

As discussed previously (see Section 2.5), there is some evidence suggesting remote effects mediated by the autonomic and somatic nervous systems following cervical spine manipulation. Specifically, reflex responses subsequent to MAM excite a relatively large pool of motor neurons both at and adjacent to the involved segment while stimulation from IAM appears to be restricted to the area of application (32). However, it is not known is if these different activation patterns results in differences in remote effects. Thus, the inclusion of grip strength and wrist blood pressure was an attempt to quantify these effects (84, 129-132)

Table 5 – Minimum clinically detectable changes for cervical range of motion (198, 199)

Flexion	Extension	Left Rotation	Right Rotation	Left Lateral Flexion	Right Lateral Flexion
6.5°	5.1°	4.9°	6.1°	4.2°	3.6°

3.3.3. Sample size calculation

Calculation of sample size was based on detecting a difference of 0.4 units in PPT levels, with

a standard deviation of 0.4, comparison of 2 means, an α of 0.05, and desired power (β) of 80%. These assumptions generated a minimum sample size of 21 participants per group and a total cohort size of 63 (96).

3.4. Study protocol and participant flow

At the intervention visit, each participant had baseline measurements taken and the stretching routine administered by LG. They were then escorted to a second room where the intervention was performed. The participant was then directed by the intervention practitioner to return to the original room where LG performed the post-intervention measurements. Due to external circumstances, both practitioners were not always present for all intervention sessions.

As mentioned above, the outcomes measured included neck pain (VAS and PPT), cervical ROM, grip strength and wrist blood pressure. A follow-up text message asking participants to report their neck pain on the NPRS was sent to all participants 7 days post-intervention. Participants were then informed that their involvement in the study had ended. Participant progression through the study is outlined in Figure 3.

3.5. Interventions

This trial involved three groups described below.

Group One:

Participants in Group 1 were required to perform a standardised active cervical stretching routine guided by LG. Each participant performed flexion, extension, left lateral flexion, right lateral flexion, left rotation and right rotation of the cervical spine to end range with each position maintained for 30 seconds and completed 3 times. The use of exercise as an active control ensured that each participant had the potential for improvement as the beneficial effects of exercise in MNP have been reported previously (1, 2, 156).

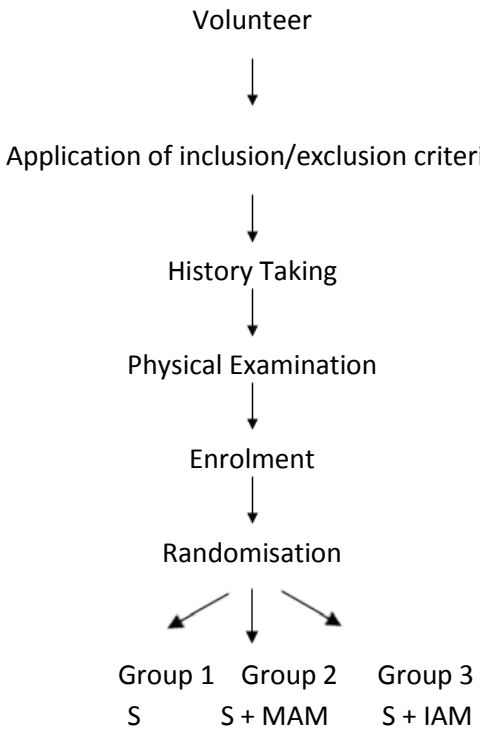
Group Two:

Participants in Group 2 performed the same stretching routine as Group 1 followed by an HVLA cervical spine manipulation (MAM). The MAM technique used was a cradle hold, index contact, lateral flexion thrust manipulation (Figure 4). In biomechanical terms, contralateral cervical rotation and homolateral lateral flexion are used to facilitate a distraction force across the cervical spine that is directed towards opening the contralateral segment at the

involved level. The thrust was applied in a lateral-medial direction, perpendicular to the cervical spine. In this instance, the side contacted by the primary hand of the practitioner is referred to as the ipsilateral side while the opposite side is referred to as the contralateral side (90, 204).

Group Three:

Participants in this group performed the same stretching routine as Groups 1 and 2 followed by an Activator® cervical spine manipulation (IAM). The IAM was delivered using an Activator® IV instrument on a setting of '2' (Figure 5). The participant was placed in the prone position while the thrust was administered to the junction of the pedicle and lamina of the involved segment in an anterior, superior and slightly medial line of drive. In this trial, the Activator® instrument was used to deliver a biomechanical force only and was not used in accordance with any other pre-determined therapeutic protocol (106).



S: stretching; MAM: manually applied manipulation; IAM: instrument applied manipulation

Figure 3 – Participant flow diagram

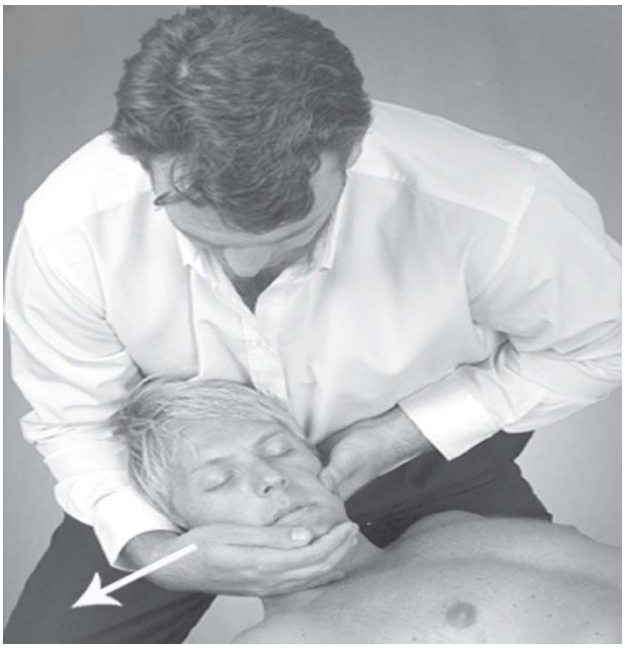


Figure 4 – MAM technique: Cradle hold, index contact, lateral flexion thrust (90)

3.6. Measuring instruments

3.6.1. Activator® IV instrument

The Activator® Adjusting Instrument, originally based on a dental impactor (106, 108, 205, 206), is a hand-held spring-loaded instrument which utilises potential energy stored in a compressed internal spring to strike an internal hammer against an anvil that propels a stylus forward (see Figure 6). The impulse force-time period of a spring-loaded Activator® has been reported to be approximately 5 milliseconds with a peak-to-peak acceleration of 6000 metres/second^2 (13, 45, 207).

Figure 5 – Activator® adjusting instrument IV (208)

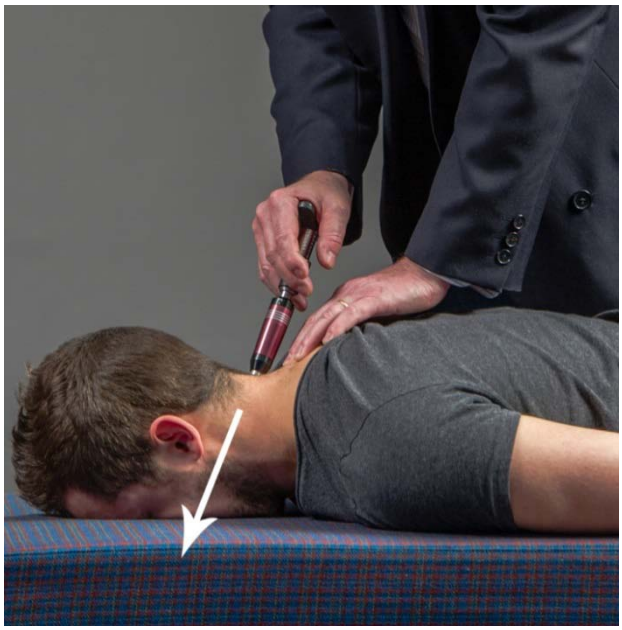


Figure 6 – IAM technique: Activator IV® instrument

3.6.2. Visual analogue scale

An eleven-point VAS scale (see Figure 7) was used to measure subjective pain levels. As discussed previously, the VAS is a commonly used tool to measure pain intensity that has been shown to have good reliability and validity (181-183).

3.6.3. Numerical pain rating scale

The numerical pain rating scale (NPRS) was sent to participants by telephone text message in the form of a question 'Out of 10, how is your neck pain today'.

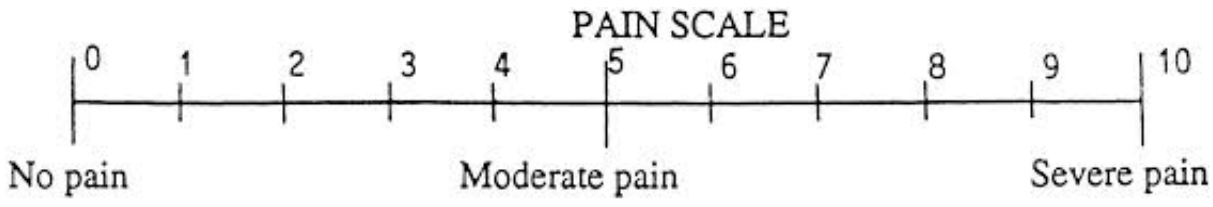


Figure 7 – Visual Analogue Scale (209)

3.6.4. Algometer

Pressure pain thresholds (PPT) were measured using a *JTech Medical Commander Algometer™ (Salt Lake City, Utah)* (see Figure 8). The instrument was placed over the spinous

process of the involved segment using a 0.5 cm^2 tip as recommended for the cervical region. Results were stored and downloaded at the end of each participant visit (16).

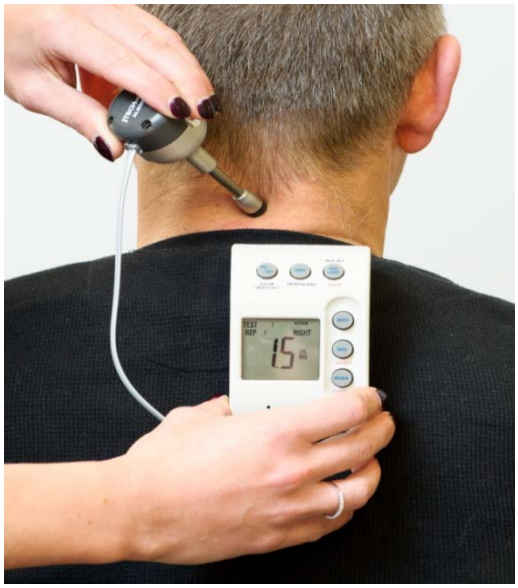


Figure 8 – JTech Medical Commander Algometer™ (16)

3.6.5. Inclinometer

The *JTech Medical Dualer IQ Pro Digital Dual Inclinometer™ (Salt Lake City, Utah)* (see Figure 9) was used to measure cervical ROM. The device has a reported accuracy and repeatability of ± 2° and can be used in either dynamic dual or static single mode. All measurements for this trial were performed in the dynamic dual mode (14).

Figure 9 – JTech Medical Dualer IQ Pro Digital Inclinometer™ (14)

3.6.6. Dynamometer

The *JTech Medical Commander Grip™ (Salt Lake City, Utah)* dynamometer (see Figure 10) was used to measure hand grip strength. The device has the ability to record and display data in digital format for up to 25 individual tests in addition to calculating the coefficient of variation for determining consistency (210).

Figure 10 – JTech Medical Commander Grip Dynamometer™ (210)

3.6.7. Sphygmomanometer

The *Sigma Medical Heine Memotronic PC2™* electronic sphygmomanometer (Herrsching, Germany) (see Figure 10) was used to measure blood pressure at the wrist. The device can store up to 250 individual measurements (15).

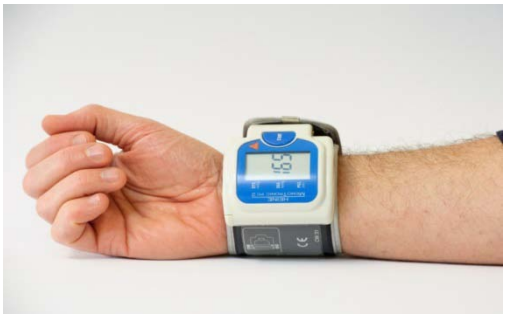


Figure 11 – Heine Memotronic PC2™ (15)

3.7. Statistical analysis

Statistical analysis was performed using MiniTab17® software. A significance level of 0.05 was used except when correction was made for multiple comparisons. One way analysis of variance using ANOVA for continuous variables (age, height, weight and PPT), the Kruskal-Wallis test for VAS and NPRS (non-normal distribution) and the Pearson's Chi-squared (x^2) test for categorical data (sex and identified painful spinal level) was performed on

participant characteristics to report on differences between groups at baseline. All results for outcome measures were analysed for normality of distribution using probability plots. Normally distributed data were analysed using ANOVA and Tukey's Honestly Different Test for multiple comparisons between groups. Analysis of data which did not have a normal distribution was performed using the Kruskal-Wallis and Mann-Whitney Tests with a Bonferroni correction for multiple comparisons between groups. Two-sample T-tests were used to compare mean differences between the intervention groups (MAM and IAM) for outcome measures stratified as ipsilateral or contralateral to side of manipulation. Participant baseline characteristics, data for group results at each time point by outcome measure and adverse events are presented in tabular form, while results comparing differences between groups were presented using box-plots.

3.8. Summary

This study was designed to investigate the relative effects of MAM and IAM cervical spine manipulation for the treatment of MNP. The interventions administered, outcomes measured, equipment used, participant recruitment and flow through the trial have been outlined in addition to the methods used for statistical analysis presented in Chapter 4.

4. Results

4.1. Characteristics of study participants

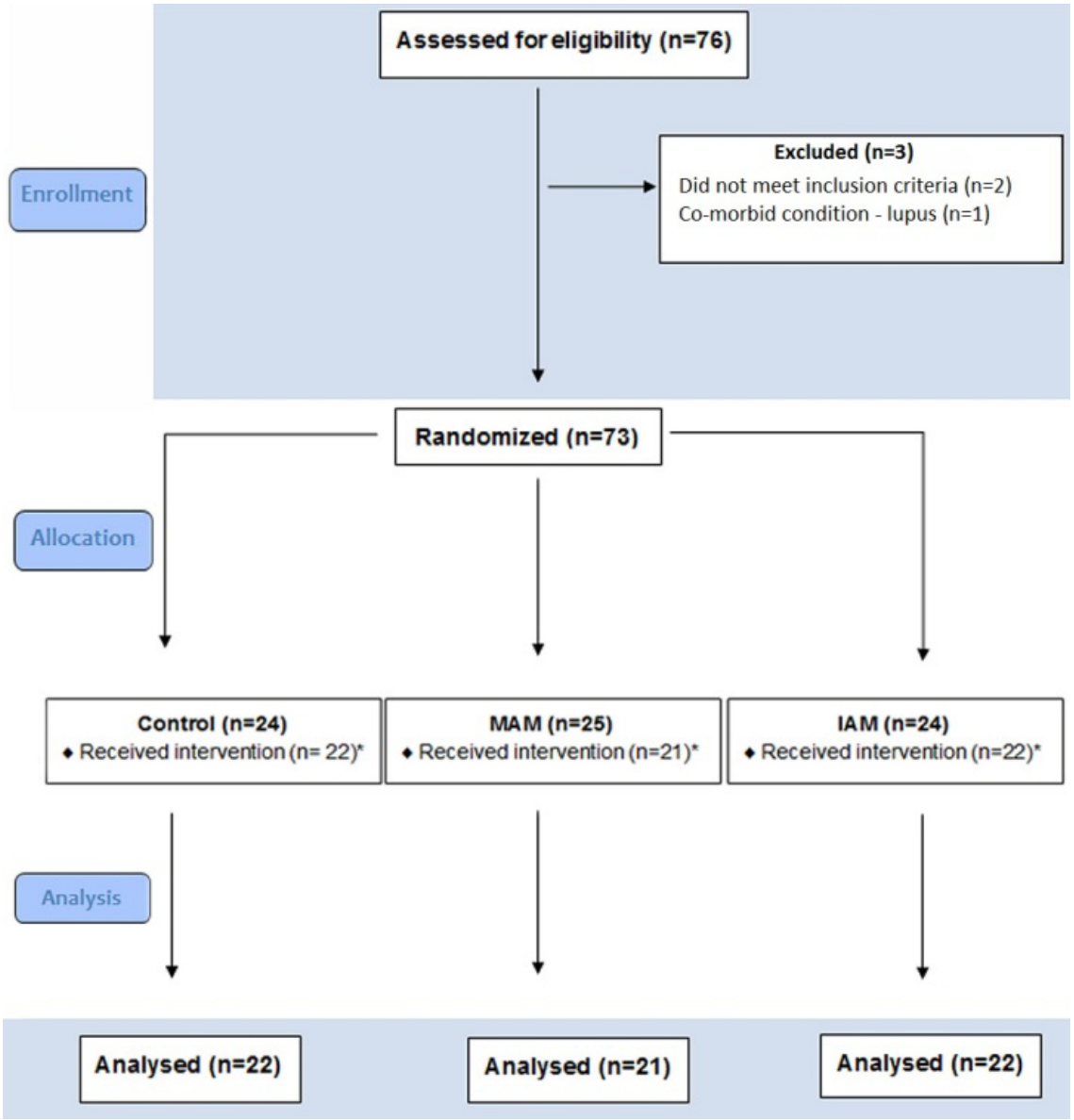
Baseline characteristics of the sixty-five participants revealed thirty-seven males (57%). The average age of the cohort was 24.4 ± 4.1 years and BMI 24.2 ± 3.6 kg/cm^2. Baseline pain levels for VAS were 3.4 ± 1.93 cm and for PPT were 4.81 ± 1.73 kg. The identified painful spinal level was: C5 on 20 occasions (30.8%); C6 on 24 occasions (36.9%); and C7 on 21 occasions (32.3%). These characteristics are presented in Table 6. All participants received the intervention to which they were assigned. No between group differences for baseline characteristics were present: age (p = 0.627); sex (p = 0.878); height (p = 0.755); weight (p = 0.810); VAS (p = 0.598); PPT (p = 0.605); and identified painful spinal level (p = 0.703).

Table 6 – Participant baseline characteristics

Participant Baseline Characteristics				
Characteristic	Control (n=22)	MAM (n=21)	IAM (n=22)	p-value
Age, y*	23.8 ± 3.5	24.4 ± 4.0	25 ± 4.9	0.627
Sex (male), n (%)	13 (59)	11 (52)	13 (59)	0.878
Height, cm*	174.0 ± 9.2	172.3 ± 8.2	174.1 ± 9.4	0.755
Weight, kg*	73.0 ± 11.4	71.7 ± 15.3	74.2 ± 10.2	0.810
VAS (baseline), cm*†	3.1 ± 2.0	3.4 ± 1.7	3.7 ± 2.1	0.598
PPT (baseline), kg*	5.08 ± 1.82	4.62 ± 1.18	4.72 ± 2.18	0.605
Identified painful spinal level, n (%)				0.703
C5	7 (32)	6 (29)	7 (32)	
C6	6 (27)	8 (38)	10 (45)	
C7	9 (41)	7 (33)	5 (23)	

VAS: visual analogue scale; PPT: pressure pain threshold; *Values are mean ± SD; † Scored on 0 – 10 scale

Participant flow through the trial is outlined in Figure 12. Seventy-six respondents were assessed for inclusion in the trial with three excluded subsequent to application of the inclusion and exclusion criteria. Of the three excluded respondents, two had recently seen a manual therapist for treatment of their neck pain and the third had been diagnosed with an auto-immune disease affecting the musculoskeletal system. Seventy-three volunteers were enrolled with eight failing to attend the intervention session or respond to communications from researchers. These non-attendees were distributed across the groups in the following way: two each for Control and IAM groups and four for the MAM group. Post-hoc analyses



*differences in allocation due to failure to attend intervention session

Figure 12 – CONSORT participant flow diagram

revealed no differences in demographic characteristics at baseline between the 73 volunteers and 65 participants: age (p = 0.076); sex (p = 0.883); height (p = 0.867); weight (p = 0.693); VAS (p = 0.584); and identified painful spinal level (p = 0.863).

4.2. Results

Table 7 shows the p-values for the significant results in the trial. Mean differences with confidence intervals for the outcome measures at each time point between groups are presented in Table 8. Table 9 shows outcome measure means for each time point. Boxplot representations of significant results are displayed in Figure 13 and are reported in the body of text, while non-significant results are provided in Appendix E (Figure 14 – 30).

Table 7 – P-values for statistically significant results

		MAM – Control (P-value, CI)	**IAM – Control** (P-value, CI)	**MAM – IAM** (P-value, CI)
VAS^	Post Rx	0.009 (0.00, 3.00)	0.064 (-0.00, 2.00)	0.484 (-2.00, -0.00)
NPRS^	7 day follow-up	0.007 (-2.68, -0.35)	0.148 (-2.06, 0.24)	0.428 (-0.56, 1.77)
Right Rotationł	Post Rx	0.109 (-0.94, 11.85)	0.957 (-7.06, 5.58)	0.059 (-12.59, 0.20)

VAS: visual analogue scale; NPRS: numerical pain rating scale; Rx: treatment; ^ Scored on 0 – 10 scale; ł: no between group differences; CI: 95% confidence interval

4.2.1. Subjective pain levels (VAS and NPRS)

One-way analysis of variance using ANOVA demonstrates a difference in subjective pain between MAM and the Control group immediately post-intervention (p = 0.009) and at 7 day follow-up (p = 0.007) (see Table 9). Figure 13 shows change in subjective pain scores by group from baseline to each time point. All groups displayed a decrease from baseline to post-intervention. These decreases were: Control (-0.5cm); MAM (-1.5cm); and IAM (-1.3cm). The initial decreases were variably reduced at 7 days in both intervention groups (MAM and IAM): MAM (-1.3cm); and IAM (-0.7cm) (see Figure 13). The Control group displayed an increase in subjective pain from baseline to 7 day follow-up (0.2cm) with no other differences between groups: Control and IAM (post-intervention [p = 0.06]; 7 day follow-up [p = 0.145]); and MAM and IAM (post-intervention [p = 0.48]; 7 day follow-up [p =0.43]).

Table 8 – Outcome measure mean changes for each time point

		Control (mean, CI)	**MAM** (mean, CI)	**IAM** (mean, CI)	**p value**
Pain	VAS^ Post Rx	-0.50 (-1.04, 0.04)	-1.48 (-2.03, -0.92)	-1.32 (-1.86, -0.78)	**0.026**
	NPRS^ 7 day follow-up	0.18 (-0.50, 0.86)	-1.33 (-2.03, -0.64)	-0.73 (-1.40, -0.05)	**0.010**
	PPT § Post Rx	-0.23 (-0.62, 0.15)	0.07 (-0.32, 0.47)	0.30 (-0.08, 0.68)	0.148
cROM (degrees)	Flexion Post Rx	4.33 (-0.19, 8.86)	-1.32 (-5.95, 3.32)	2.83 (-1.70, 7.36)	0.206
	Extension Post Rx	-1.20 (-5.72, 3.32)	-0.00 (-4.63, 4.63)	-3.14 (-7.66, 1.38)	0.621
	Left Rotation Post Rx	-1.56 (-6.39, 3.27)	5.11 (0.16, 10.06)	-1.61 (-6.44, 3.23)	0.092
	Right Rotation Post Rx	-1.52 (-5.23, 2.20)	3.94 (0.13, 7.74)	-2.26 (-5.98, 1.46)	**0.047**
	Left Lateral Flexion Post Rx	0.17 (-3.25, 3.52)	0.84 (-2.62, 4.31)	-4.21 (-7.60, -0.83)	0.084
	Right Lateral Flexion Post Rx	1.00 (-1.67, 3.66)	-2.82 (-5.55, -0.10)	-0.53 (-3.19, 2.13)	0.140
Grip Strength (kg)	Left Post Rx	-4.46 (-6.82, -2.09)	-2.17 (-4.60, 0.25)	-1.27 (-3.64, 1.09)	0.156
	Right Post Rx	-2.99 (-6.08, 0.11)	-3.02 (-6.19, 0.15)	0.81 (-2.29, 3.90)	0.144
Blood Pressure (mmHg)	Systole Post Rx	-6.48 (-11.19, -1.78)	-1.10 (-5.91, 3.72)	-5.67 (-10.37, -0.97)	0.236
	Diastole Post Rx	-1.76 (-5.40, 1.88)	-2.57 (-6.30, 1.15)	2.77 (-0.87, 6.41)	0.093

VAS: visual analogue scale; NPRS: numerical pain rating scale; PPT: pressure pain threshold; Rx: treatment; ^ Scored on 0 – 10 scale; § measured in kg/cm^2; CI: 95% confidence interval

4.2.2. Pressure pain threshold

Changes in pressure pain threshold (PPT) for both the MAM ($0.1kg/cm^2$) and IAM ($0.3kg/cm^2$) groups increased compared to Control which decreased ($-0.2kg/cm^2$) (see Figure 14, Appendix F). However, there was no difference between groups (p = 0.148).

4.2.3. Cervical range of motion

Figure 15 shows an increase in flexion for the Control (4.3°) and IAM (2.8°) groups and a decrease in the MAM group (-1.3°). A decrease in extension was seen with all groups: Control (-1.2°); MAM (-0.0°); and IAM (-3.1°) (see Figure 16).

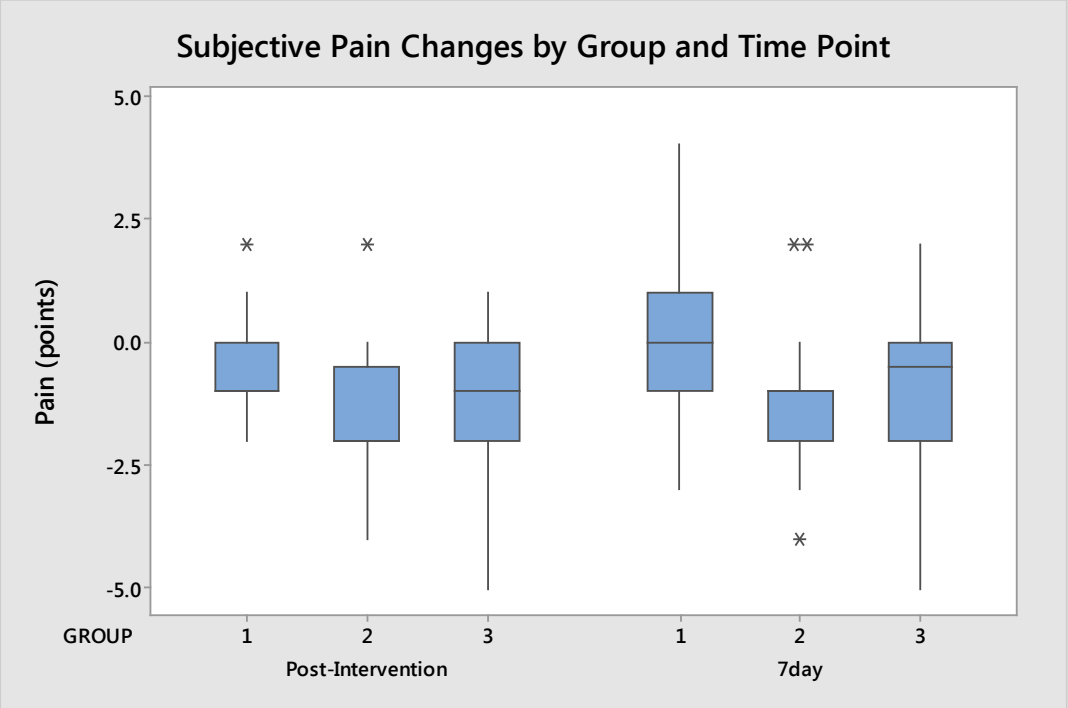
Table 9 – Outcome measures means for each time point

		Control (mean, SE)	**MAM** (mean, SE)	**IAM** (mean, SE)
Pain	VAS^			
	Baseline	3.09 ± 2.04	3.57 ± 1.60	3.68 ± 2.15
	Post Rx	2.59 ± 1.71	2.10 ± 1.81	2.36 ± 1.94
	NPRS^			
	7 day follow-up	3.27 ± 2.03	2.24 ± 1.73	2.95 ± 2.48
	PPT §			
	Baseline	5.58 ± 2.02	5.07 ± 1.28	5.16 ± 2.36
	Post Rx	5.35 ± 1.70	5.15 ± 1.24	5.46 ± 2.36
cROM (degrees)	Flexion			
	Baseline	54.58 ± 13.52	64.41 ± 11.22	59.30 ± 12.52
	Post Rx	59.18 ± 12.40	63.10 ± 13.73	62.14 ± 11.64
	Extension			
	Baseline	68.27 ± 14.26	63.92 ± 10.24	61.27 ± 12.34
	Post Rx	67.08 ± 14.14	63.92 ± 9.54	58.14 ± 10.26
	Left Rotation			
	Baseline	61.55 ± 9.45	63.92 ± 13.42	61.88 ± 11.84
	Post Rx	59.98 ± 7.90	69.03 ± 14.34	60.27 ± 9.59
	Right Rotation			
	Baseline	59.62 ± 9.61	65.05 ± 14.76	60.32 ± 10.88
	Post Rx	58.11 ± 9.79	68.98 ± 11.56	58.06 ± 10.11
	Left Lateral Flexion			
	Baseline	44.70 ± 10.13	44.92 ± 10.70	45.24 ± 7.93
	Post Rx	44.83 ± 8.51	45.76 ± 9.58	41.03 ± 6.38
	Right Lateral Flexion			
	Baseline	42.21 ± 8.08	44.78 ± 8.79	41.17 ± 7.29
	Post Rx	43.21 ± 8.44	41.95 ± 8.46	40.64 ± 6.39
Grip Strength (kg)	Left			
	Baseline	80.96 ± 26.97	73.64 ± 28.30	77.27 ± 26.23
	Post Rx	76.50 ± 25.60	71.46 ± 26.88	76.00 ± 27.30
	Right			
	Baseline	89.32 ± 21.75	79.57 ± 26.43	83.30 ± 31.36
	Post Rx	86.33 ± 19.51	76.56 ± 25.23	84.11 ± 33.11
Blood Pressure (mmHg)	Systole			
	Baseline	136.33 ± 12.39	138.27 ± 18.21	138.71 ± 15.59
	Post Rx	129.85 ± 11.90	137.18 ± 12.44	133.04 ± 15.59
	Diastole			
	Baseline	91.36 ± 10.30	93.94 ± 11.58	91.71 ± 10.21
	Post Rx	89.6 ± 17.48	91.36 ± 10.45	94.49 ± 13.08

VAS: visual analogue scale; NPRS: numerical pain rating scale; PPT: pressure pain threshold; Rx: treatment; ^ Scored on 0 – 10 scale; § measured in kg/cm^2

Figure 17 shows an increase in left rotation in the MAM group (5.1°) and a decrease in both the Control (-1.6°) and IAM (-1.6°) groups. Figure 18 shows an increase in right rotation in the MAM (3.9°) group and a decrease in the Control (-1.5°) and IAM (-2.3°) groups. Figure 19 shows an increase in left lateral flexion in the Control (0.1°) and MAM (0.8°) groups and a decrease in the IAM group (-4.2°). Figure 20 shows an increase in right lateral flexion in the

Control group (1.0°) and a decrease in the MAM (-2.8°) and IAM (-0.5°) groups. However, none of these changes were significant: flexion (p = 0.206); extension (p = 0.621); left rotation (p = 0.092); and right rotation (p = 0.047). There were also no significant between-group differences: left lateral flexion (p = 0.084) and right lateral flexion (p = 0.140). Figure 21 shows an increase in ipsilateral (4.6° ± 15.06) and contralateral (4.4° ± 9.56) rotation on the side of manipulation in the MAM group. Figure 22 shows a decrease in ipsilateral (-2.7° ± 8.76) and contralateral (-1.2° ± 8.94) rotation on the side of manipulation in the IAM group. Figures 23 and 24 show a decrease in lateral flexion on the ipsilateral and contralateral sides following either intervention: [ipsilateral: -1.8° ± 10.30 (MAM) and -1.73° ± 6.90 (IAM); contralateral: -0.2° ± 7.76 (MAM) and -3.0° ± 6.50 (IAM)]. However these changes were not significant: [ipsilateral rotation (p = 0.062); contralateral rotation (p = 0.055); ipsilateral lateral flexion (p = 0.990); contralateral lateral flexion (p = 0.209)].



Pre-Post: change from baseline to immediately post-intervention; Pre-7day: change from baseline to 7 day follow-up

Figure 13 – Subjective pain changes by group and time point

4.2.4. Grip strength

Figure 25 shows decreased left grip strength for all groups: Control (-4.5kg); MAM (-2.2kg); and IAM (-1.2kg). Figure 26 shows an increase in right grip strength in the IAM group (0.8kg)

and a decrease in the Control (-3.0kg) and MAM (-3.0kg) groups. However, these changes were not significant for left (p= 0.156) or right grip strength measurements (p = 0.144).

Figure 27 shows that in the IAM group, grip strength increased on the side contralateral to manipulation (0.5kg ± 14.30) and decreased on the side ipsilateral to manipulation (-1.5kg ± 15.36). Figure 28 shows a decrease in grip strength in the MAM group on both the ipsilateral (-4.5kg ± 10.50) and contralateral (-6.7kg ± 15.18) side of manipulation. These changes were not significant for either ipsilateral or contralateral grip strength: ipsilateral (p = 0.460); contralateral (p =0.107).

4.2.5. Wrist blood pressure

Figure 29 shows an increase in diastole in the IAM group (2.8mmHg) and a decrease in the Control (-1.8mmHg) and MAM (-2.6mmHg) groups. Figure 30 shows a decrease in systole for all groups: Control (-6.5mmHg); MAM (-1.1mmHg); and IAM (-5.7mmHg). However, none of these changes were significant for either systole (p = 0.236) or diastole (P =0.093).

4.3. Adverse events

There were eight adverse events reported in the trial (see Table 10). All were classified as mild (170). Four were reported in the Control group, one in the MAM group and three in the IAM group.

Table 10 – Adverse effects

	Control	MAM	IAM
Stiffness	X		
Mild soreness	X	X	X
Sore with movement	XX		
Felt 'unbalanced' due to only one side manipulation*			X
Neck clicking since manipulation*			X

Adverse events are represented by an X; *participant reported being concerned about this reaction but there was no increase in pain

4.4. Summary

The results from this trial show that MAM decreases subjective pain levels both immediately post-intervention and at 7 day follow-up in people with MNP. However, pressure pain

thresholds are not altered by either MAM or IAM. In addition to this, there were no changes in cervical ROM, grip strength or wrist blood pressure following intervention (MAM or IAM). Eight minor, transient adverse events were reported in the trial. A detailed discussion of these results follows in Chapter 5.

5. Discussion

5.1. Introduction

This trial of 65 participants between the ages of 18-35 years with MNP reported that MAM decreased subjective pain levels both immediately post-intervention and at 7 day follow-up.

5.2. Primary outcome measures

5.2.1. Subjective pain levels (VAS and NPRS)

Subjective pain levels decreased in the MAM group compared to the Control ($p = 0.009$) and IAM ($p = 0.484$) groups. This continued at 7 day follow-up where less pain was also reported by participants in the MAM group ($p = 0.007$) compared to Control (see Table 9). During this period subjective pain measurements increased from baseline in the Control group. It is possible this increase may have been the result of incomplete blinding and the absence of a validated control intervention. The validation of an active control intervention in manual therapy is not without its problems (211-213). Two important objectives of an active control intervention should be: 1) the equalisation of the non-specific effect of physical touch between groups; and 2) the blinding of the participant to the nature of the treatment (21, 155, 214). The issues that accompany non-blinding include altered participant expectation, equivalence of effectiveness between the arms of the trial and perceived clinical effect. In situations of non-blinding in the control group conclusions based on the results for the intervention groups must be tempered as it is not known how non-blinding may have affected the results. In the reporting of subjective outcome measures (e.g. VAS/NPRS) the blinding of participants is particularly important as knowledge of group allocation and perception of that treatment's effect may influence both psychological and physical responses (52, 215-217).

There is some support for the results from the current study in the literature. Martinez-Segura *et al* reported a decrease in subjective pain levels following a single cervical HVLA manipulation compared to a control mobilisation in participants with MNP (73). Snodgrass *et al* reported greater reductions in subjective pain levels (VAS) with higher force (90 N) mobilisation compared to both a lower force (30 N) mobilisation and a control of detuned laser (49). However, Dunning *et* al reported increased subjective pain levels subsequent to upper cervical and thoracic manipulation compared to mobilisation (154).

The MCID for VAS has been reported as being in the range of 1.7 to 2.1 cm (184, 185) while the MCID for NPRS is 1.3 (188). As none of the groups in the current study achieved this level of change, the results cannot be considered clinically significant. This is in contrast to Saavedra-Hernandez *et al* who reported clinically significant decreases for VAS following cervical spine manipulation for chronic MNP (147). Use of subjective outcome measures such as VAS to measure changes in pain requires consideration of factors such as patient satisfaction and expectation with respect to treatment outcomes (218, 219). Other factors that may influence the rating of current pain include the ability to carry out daily routines, comparison with usual pain, distress caused by the pain and how current pain compares to the worst pain ever (220). In addition to these, interpretation of VAS and NPRS can vary between individuals. For example, some patients interpret the minimum endpoint (labelled '0') as indicative of 'normal' or 'manageable' pain. These patients often exclude the lower half of the scale as they consider these levels of pain outside their experience. Interpretation of the VAS in this way results in an inflated score as these patients only use the upper end of the range (6 – 10) (186, 220). This has led some authors to question the validity of the scale (181-183, 219, 221). This process may have occurred in the current trial where reported VAS did not appear to be consistent with expected levels of disability as measured by physical examination.

In addition to this, it has been reported that patients may concurrently hold different interpretations of the same set of instructions (222, 223). As a result, an inconsistent understanding of the standard question 'Out of 10 how is your neck pain today?' may have influenced the 7 day follow-up NPRS results as a participant may have interpreted the question to mean average pain over the previous week.

5.2.2. Pressure pain threshold

There were no differences in PPT between groups immediately post-intervention. This finding is consistent with results from other studies. Snodgrass *et al* found no difference in PPT following high and low force mobilisation in people with chronic, non-specific neck pain (49). Sterling *et al* reported no difference in PPT between lateral-glide mobilisation and placebo in participants with whiplash (224). In addition to this, none of the reported changes in the current trial achieved the MCID for PPT (1.77kg/cm^2) (180). This finding is also consistent with Martinez-Segura *et al* who found that although PPT increased with both

cervical and thoracic manipulation, the changes were not significant (73). Interestingly, in this trial PPT decreased in the Control group (stretching) only. A possible explanation for this may be that as MNP is defined as neck pain exacerbated by movement, repetitive stretching *i.e.* repetitive movement, may have increased pain levels and resulted in a decrease in PPT.

There are a number of other reasons that may explain the absence of any clinically meaningful change in PPT in this trial. Firstly, there was no inter-examiner validation of the initial diagnosis of MNP or level of dysfunction in the neck. It is possible that an incorrect diagnosis may have influenced the results. Notwithstanding this, a recent study supports the use of a targeted physical examination involving pain provocation with manual palpation for accurate diagnosis of MNP (225). Secondly, as the MAM and IAM practitioners were blinded to the spinal level of dysfunction diagnosed, the intervention may not have been administered to the same segment used to measure PPT. Thirdly, there was heterogeneity in the level treated between the two groups: the MAM group received manipulation to C5/6 while IAM was administered from levels C5-C7. In addition to this, participants were naïve to PPT and were not familiarised with the measurement prior to assessment (e.g. measurement at a site distal to the cervical spine). This introduced the possibility of inaccurate reporting for the initial PPT measurement as the participant was uncertain of what they were expected to describe (*i.e.* first sensation of discomfort). Participant description of PPT varied considerably and included descriptors such as 'pain', 'tightness', 'pinch', 'pressure' and 'change in sensation'. These descriptions suggest individuals may experience pain differently and this inconsistency in reporting may have adversely affected PPT results in this trial. Inconsistent descriptions were recognised early in the trial and LG attempted to provide participants with an exhaustive explanation of the sensations which may be experienced. Participants were encouraged to report on the same sensation they reported at the initial assessment.

5.3. Secondary outcome measures

5.3.1. Cervical range of motion

A possible explanation for the absence of any reported changes in cervical ROM in this trial may be related to the difference in biomechanics between MAM and IAM. The MAM technique used in this trial facilitated distraction and physical displacement of the cervical spine with the force directed toward opening the contralateral side. The IAM technique did

not result in gross cervical displacement. The role of pre-load manipulative forces in eliciting positive changes has been reported in the literature (32, 47, 48, 56). IAM pre-load forces are variable (50, 56) and may not generate sufficient force to elicit positive changes (47). Furthermore, it has been proposed that the effects of transmitted loads (seen with IAM), may be different to applied loads (MAM) due to the effects of patient pre-positioning and contributions from both inertia and the active and passive properties of intervening tissues (33). It is reasonable to expect that increased muscle tension absorbs a proportion of the applied force resulting in a diminished level of force reaching the mechanoreceptors of the joint being manipulated. Furthermore, it has been suggested that co-activation may partially explain the complex neurophysiological response to joint manipulation (58). A threshold of applied force (40 N) has been reported as being necessary to elicit co-activation (59). As MAM and IAM apply approximately 100 and 40 N respectively, it is possible that both may elicit co-activation. . Reflex responses subsequent to MAM are reported to excite a relatively large pool of motor neurons both at and adjacent to the involved segment while IAM stimulation is thought to be restricted to the area of application (32).

In addition to this, different levels of vertebral displacement have been reported subsequent to application of the two techniques. MAM applied to the lumbar spine results in approximately 10mm of linear displacement (33, 60) while the changes associated with IAM range from 0.07 to 0.81mm (61). Although the extent of linear displacement in the cervical spine has not been reported in the literature, it is reasonable to expect it to be less than in the lumbar spine as the forces exerted during cervical manipulation are less than in lumbar manipulation (39).

To place the current results in context, Snodgrass *et al* and Martinez-Segura *et al* report no change to cervical ROM following cervical mobilisation and manipulation in populations with MNP (49, 73). Additionally, a recent systematic review reported uncertainty as to whether spinal manipulation improves cervical ROM (195). Highlighting this uncertainty are other reports of both no change (49, 226) and change (227) following mobilisation and manipulation.

Measuring cervical ROM has been reported in the literature as having good intra- and inter-observer reliability (28, 195, 228). The precision and repeatability of the inclinometer tool

used in this trial are congruent with those published in the literature suggesting that the measurements taken in this trial were accurate (28, 229-231).

5.3.2. Grip strength

Grip strength decreased in all groups except on the right following IAM. However, this change was not significant. Nitschke *et* al suggests that a difference of 6kg is necessary to detect a real change in grip strength in a healthy population (202). There are no reports of grip strength MCID for symptomatic populations such as those with MNP therefore, based on Nitschke's recommendation, none of the changes reported in the current study were clinically significant. As each participant was required to complete three maximal efforts over a short period of time, it is possible that the observed decreases may have been due to fatigue rather than as a result of any intervention. However, several studies using a similar design to the current trial reported that fatigue did not affect results (200, 232, 233). The findings of this study are in contrast to those reported by Botelho and Andrade who reported increased grip strength following cervical manipulation (131). A possible explanation for this difference may be related to heterogeneity between the cohorts studied. The cohort examined by Botelho consisted of asymptomatic elite judo athletes while the current study investigated MNP in a non-athletic population. This difference is salient as the literature reports that work and leisure activities are highly influential on grip strength (234, 235).

5.3.3. Wrist blood pressure

There were no significant changes in systolic or diastolic blood pressure between groups. For blood pressure, MCID has been defined as 'the minimum reduction in cardiovascular risk that the patient feels outweighs the inconvenience, costs and side effects of antihypertensive therapy' (203). Several factors have been reported as capable of varying blood pressure. These include: respiration, emotion, exercise, meals, tobacco, alcohol, temperature, bladder distension, pain, age, race and circadian patterns (236). Prior to measurement of blood pressure, it is recommended that patients should be relaxed in a quiet room at a comfortable temperature with a short period of rest (236, 237). These conditions were not present in the current study nor were participants instructed to refrain from the consumption of caffeine (238), pre-exercise supplements (239), or a meal (239)

prior to attendance at the intervention session. These factors may have elevated blood pressure and altered the reported measurements. The lack of change in blood pressure following cervical manipulation in this trial may therefore have had a temporal rather than causal relationship. The theory of 'white coat' syndrome with respect to blood pressure has been reported in the literature as having the potential to contribute to raising blood pressure by as much as 90mmHg (236, 237, 240). It is possible that some participants may have been anxious about having both their blood pressure measured as well as receiving a cervical manipulation. Many participants reported never having received spinal manipulation and as such may have been unsure of what to expect. In addition to these factors, several participants reported undertaking an exercise session immediately prior to attending the intervention session and as exercise has the potential to lower both systolic and diastolic blood pressure this may have affected blood pressure readings (241-243). Furthermore, inherent variability within individuals due to natural diurnal variation may also have contributed to the changes measured in the trial (244).

5.4. Adverse events

In a recent trial investigating manipulation (MAM and IAM) and mobilisation, Gemmell *et al* reported fifteen adverse events (120). These findings are similar to the current study which reported eight minor, transient adverse events. Interestingly, the Control (stretching) group experienced more adverse events than the MAM or IAM groups. It is possible that participants in the Control group may have perceived their group allocation negatively resulting in a nocebo effect. In addition to this, participants who had previously received spinal manipulation may have had different expectations of treatment, resulting in the reporting of adverse events based on past experience. Participants naïve to cervical manipulation may have viewed a minor adverse event more negatively compared to those who had previously experienced spinal manipulation. The MAM and IAM groups reported equal numbers of minor adverse events while two participants in the IAM group reported symptoms that were uncommon. These symptoms were 'feeling unbalanced as both sides of the cervical spine had not been manipulated' and 'increased neck clicking since manipulation'. While these may not be considered 'true' adverse events, they were included in the count so as to provide a complete record of all reported effects. In addition to the above, as the Activator® instrument has a mechanical, surgical appearance and produces a

'clicking' noise, participants may have perceived it as potentially harmful, resulting in an additional nocebo effect (120).

Considering the frequency of adverse events reported in this study, cervical manipulation appears to be a safe intervention for adults with MNP.

5.5. Limitations

5.5.1. Internal validity

A high level of internal validity is achieved by adopting a structured and controlled methodology in which bias is minimised. While the influence of the participant-therapist interaction on internal validity is unknown, it can be described in terms of the Rosenthal and Hawthorne effects (245). The Rosenthal Effect is a phenomenon where results of an experiment may be inadvertently altered by a therapist who conveys their personal expectations about specific outcomes related to a certain treatment. Conversely, the Hawthorne Effect occurs when participants alter their behavior as a result of the knowledge that they are being observed during the trial (246).

Blinding of participants and practitioners minimises performance bias (247, 248). However, there was inadequate blinding of both participants and practitioners in the current trial suggesting performance bias may have occurred. Several authors report that participant expectation of benefit influences treatment outcomes (52, 249, 250). As the trial investigated the effects of spinal manipulation, it is possible that participant non-blinding may have resulted in a perceived increased positive effect (placebo) in participants who received spinal manipulation while those in the Control group may have had a negative perception of the effect of stretching compared to manipulation (215-217). Failure to acknowledge the limitations of this type of bias raises the possibility of a Type I error (214). In the absence of an effective control procedure, the trial may have failed to account for non-specific mechanisms such as a placebo effect that may have been associated with neurophysiological responses to manipulation (52, 53, 214, 251). However, the current literature does not report a validated 'sham' manipulation procedure for the cervical spine that could be used as a control in the trial (212, 213). Furthermore, the ethics of clinical research calls for 'equipoise' *i.e.* genuine uncertainty regarding the effectiveness of a treatment on the part of the investigators (252). In the current trial, inclusion of an active rather than sham control group was an attempt to uphold this principle as stretching has

been reported as an effective treatment for MNP (2, 4).

Detection bias occurs with inadequate blinding of the outcome assessor. Blinding of outcome assessors reduces the risk of introducing this type of bias into the results (121, 122). Detection bias may have been present in this study due to inadequate blinding of the outcome assessor (LG). This was due to differences in practitioner availability at certain times during the trial i.e. at certain times only one practitioner was available to administer treatment. As this trial was conducted as part of a Master of Research degree with limited funding, the research student (LG) assumed the responsibility of recruiting, screening and examining participants, scheduling, implementation of the stretching routine and measurement of baseline and post-intervention outcome measurements and was therefore not blinded to group allocation.

Although the same wording, time frame and format were used in the application of both subjective pain measures, it is a methodological limitation that two pain scales (VAS and NPRS) were used (186). As discussed previously, patients interpret pain scales in different ways (see Section 5.2.1) and although both that are used in this trial are commonly used, it is possible this inconsistency may have influenced the trial results.

5.5.2. External validity

Despite being the 'gold standard' in clinical research (215, 253, 254), an RCT investigates participant responses to interventions applied in an artificial setting which may not adequately reflect clinical practice (245, 255, 256). Participant response may be influenced by several factors including the participant-therapist relationship, placebo effect and participant preference. In addition to these, the impact of a participant's expectation of treatment outcomes has been suggested as a possible factor that can influence their response (52, 249, 250). The results of this study are limited to the short-term effects of a single application of cervical spinal manipulation. It has been accepted that the effectiveness of a single manual therapy interventions can produce clinically significant changes (257-260). There are two features of a single-session clinical trial that make it an attractive design. Firstly, the trial can be considered as 'proof of principle' by indicating whether a single dose is capable of achieving change. This permits the direct measurement of dose-response mechanisms for spinal manipulation which is recommended by several authors (47, 48, 50, 56).

Secondly, clinical guidelines for the management of MNP typically report multi-modal intervention over multiple sessions (2, 4). As the current study was designed to investigate the immediate effects of a single application of two different techniques, it is not surprising that the changes reported do not reflect those expected in clinical practice. Additionally, Saavedra-Hernandez *et al* reported that treating several regions (e.g. mid-cervical, cervico-thoracic and thoracic) resulted in greater reductions in disability than treating a single region (147). This suggests the presence of a cumulative dose-response mechanism. Furthermore, the current study diverges from clinical practice as the decision to apply a specific cervical manipulation did not include practitioner and participant preferences or clinical prediction rules identifying participants who were more likely to respond positively to treatment. Clinical prediction rules for MNP suggest a number of factors that can be used to identify patients who will respond positively to cervical manipulation (261, 262). In the current trial, participants were screened for exclusion based on the presence of a predetermined list of co-morbid conditions. Therefore, it is possible that participants who would not have been expected to respond positively to cervical manipulation were included in the trial.

As participants in the trial were young and displayed low baseline pain, the results may not be generalisable to older patients or those with higher levels of pain. Additionally, as participants were asked to comment on how they believed their neck pain influenced activities of daily living rather than complete a disability questionnaire, it is unknown precisely what the baseline level of disability present in the sample was and if this changed as a result of participating in the trial. As such, it is not possible to compare the level of disability of participants in this trial to other cohorts. Furthermore, the current findings may not be applicable to patients with other cervical complaints such as neck trauma or radiculopathy as participants displaying these co-morbid conditions were excluded from the trial. As all MAM and IAM interventions were administered by experienced practitioners, and significant inter-operator inconsistencies such as practitioner training, morphology and variation in the application of the MAM and IAM have been reported in the literature, it is possible that the current results may not be replicated by other researchers.

Furthermore, as this study used approximate values from the literature (39) and did not directly measure force magnitude of MAM and IAM which are reported to vary among therapists (47-49) it is possible that results obtained during the trial may not be repeatable with different practitioners.

6. Conclusion

This thesis investigated the relative efficacy of two techniques of cervical manipulation. Previous studies comparing the effect of these two techniques for the treatment of MNP were of low quality and therefore limited in their conclusions regarding the effects of manipulation.

The trial research question 'Is there a difference in efficacy between MAM and IAM cervical spine manipulation for MNP?' was answered in the affirmative by the results from an RCT which showed that MAM achieved significant changes in subjective pain levels while IAM did not.

However, there were no differences between the two techniques for PPT, cervical ROM, grip strength or blood pressure. Biomechanical factors not investigated in the trial such as peak force, pre-load force, amplitude and acceleration of the thrust in addition to the trial not reflecting current primary care treatment for MNP may have contributed to these results.

While this thesis addressed the broad issue of efficacy of different treatment techniques, it raised a number of other questions which could form the basis for future research. These include: What is the optimal threshold of force required to affect change following manipulation? What is the efficacy of other manipulation techniques? Is there a cumulative effect of multiple intervention sessions? What is the comparative effect of MAM and IAM on the same participant? What are the long-term effects of spinal manipulation? Does the effect of spinal manipulation differ in other regions of the spine?

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Appendix A

MACQUARIE UNIVERSITY

Office of the Deputy Vice-Chancellor (Research)

Research Office
C5C Research HUB East, Level 3, Room 324
MACQUARIE UNIVERSITY NSW 2109 AUSTRALIA

Phone **+61 (0)2 9850 4194**
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Email ethics.secretariat@mq.edu.au

21 July 2014

Dr Roger Engel
Department of Chiropractic
Faculty of Science
Macquarie University
NSW 2109

Dear Dr Engel

RE: *The Effect of Spinal Manipulative Therapy (SMT) on Mechanical Neck Pain*

Thank you for submitting the above application for ethical and scientific review. Your application was originally considered by the Macquarie University Human Research Ethics Committee (HREC (Medical Sciences)) at its meeting on 27 March 2014 and by the Scientific Subcommittee out of session. Further information was requested to be reviewed by the HREC (Medical Sciences) Executive.

The requested information was received via the online Human Ethics Application Form on 27 April 2014 & 03 June 2014.

I am pleased to advise that ethical and scientific approval has been granted for this project to be conducted at:

- Macquarie University

This research meets the requirements set out in the *National Statement on Ethical Conduct in Human Research* (2007 – Updated March 2014) (the *National Statement*).

Details of this approval are as follows:

Reference No: 5201400281

Approval Date: 21 July 2014

The following documentation has been reviewed and approved by the HREC (Medical Sciences):

Documents reviewed	Version no.	Date
Macquarie University Online Human Ethics Application Form	1.0	07 March 2014
Correspondence from Dr Engel responding to the issues raised by the HREC (Medical Sciences)		Received from 22/04/2014
Research Protocol	3.0	24/05/2014
MQ Participant Information and Consent Form (PICF) entitled The Effect of Spinal Manipulative Therapy on Mechanical Neck Pain	3.0	24/05/2014

Advertisement: Recruitment Invitation	3.0	24/05/2014

This letter constitutes ethical and scientific approval only.

Standard Conditions of Approval:

1. Continuing compliance with the requirements of the *National Statement,* which is available at the following website:

http://www.nhmrc.gov.au/book/national-statement-ethical-conduct-human-research

2. This approval is valid for five (5) years, subject to the submission of annual reports. Please submit your reports on the anniversary of the approval for this protocol.

3. All adverse events, including events which might affect the continued ethical and scientific acceptability of the project, must be reported to the HREC within 72 hours.

4. Proposed changes to the protocol must be submitted to the Committee for approval before implementation.

It is the responsibility of the Chief investigator to retain a copy of all documentation related to this project and to forward a copy of this approval letter to all personnel listed on the project.

Should you have any queries regarding your project, please contact the Ethics Secretariat on 9850 4194 or by email ethics.secretariat@mq.edu.au

The HREC (Medical Sciences) Terms of Reference and Standard Operating Procedures are available from the Research Office website at:

http://www.research.mq.edu.au/for/researchers/how_to_obtain_ethics_approval/human_research_ethics

The HREC (Medical Sciences) wishes you every success in your research.

Yours sincerely

Professor Tony Eyers
Chair, Macquarie University Human Research Ethics Committee (Medical Sciences)

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research* (2007) and the *CPMP/ICH Note for Guidance on Good Clinical Practice.*

Print

Appendix B

Close

Your ACTRN (registration number): ACTRN12614000804684

From: **info@actr.org.au**
Sent: Tuesday, 29 July 2014 5:18:42 PM
To: lindsay.gorrell@students.mq.edu.au

Dear Lindsay Gorrell,

Re: The Effect of Spinal Manipulative Therapy on Non-Specific (Mechanical) Neck Pain

Thank you for submitting the above trial for inclusion in the Australian New Zealand Clinical Trials Registry (ANZCTR).

Your trial has now been successfully registered and allocated the ACTRN:
ACTRN12614000804684

Web address of your trial: http://www.ANZCTR.org.au/ACTRN12614000804684.aspx
Date submitted: 22/07/2014 10:12:58 AM
Date registered: 29/07/2014 5:18:20 PM
Registered by: Lindsay Gorrell

If you have already obtained Ethics approval for your trial, could you please send the ANZCTR a copy of at least one Ethics Committee approval letter? A copy of the letter can be sent to info@actr.org.au (by email) OR (61 2) 9565 1863, attention to ANZCTR (by fax).

Please be reminded that the quality and accuracy of the trial information submitted for registration is the responsibility of the trial's Primary Sponsor or their representative (the Registrant).
The ANZCTR allows you to update trial data, but please note that the original data lodged at the time of trial registration and the tracked history of any changes made will remain publicly available.

The ANZCTR is recognised as an ICMJE acceptable registry (http://www.icmje.org/faq.pdf) and a Primary Registry in the WHO registry network (http://www.who.int/ictrp/network/primary/en/index.html).

If you have any enquiries please send a message to info@actr.org.au or telephone +61 2 9562 5333.

Kind regards,
ANZCTR Staff
T: +61 2 9562 5333
F: +61 2 9565 1863
E: info@actr.org.au
W: www.ANZCTR.org.au

Appendix C

MACQUARIE UNIVERSITY

DO YOU HAVE LOWER NECK PAIN?

Researchers from the Department of Chiropractic at Macquarie University are investigating the effect of neck manipulation on mechanical neck pain.

We are looking for people who are:

1. 18 to 35 years old
2. Have at least a one month history of mechanical neck pain in the lower neck
3. Have not had neck manipulation within the preceding month
4. Are not pregnant

How often do you need to attend?

Two visits in total (45 minutes each) over a two week period on campus at Macquarie University

Reply to a phone text message 7 days following the 2nd visit

All neck manipulations are administered by experienced chiropractors.

For more information, please contact:

Ms Lindsay Gorrell on: lindsay.gorrell@students.mq.edu.au OR

Dr Roger Engel on: roger.engel@mq.edu.au or 9850 6387

Appendix D

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Department of Chiropractic Outpatient Clinic

Title	The Effect of Spinal Manipulative Therapy on Mechanical Neck Pain
Short Title	SMT and Mechanical Neck Pain
Protocol Number	1
Project Sponsor	Department of Chiropractic, Macquarie University
Principal Investigator	Dr Roger Engel
Associate Investigator(s)	Lindsay Gorrell
Location	3 Innovation Road, Macquarie University, 2109

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you have neck pain that is mechanical in origin. The project is designed to measure the effect of neck manipulation on mechanical neck pain.

This Participant Information Sheet/Consent Form tells you about the research project. It explains what is involved which will help you decide if you want to take part in the research. Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part. If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read

• Consent to take part in the research project

• Consent to have treatments that are described

• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

There is a growing body of evidence to suggest that spinal manipulation is effective in managing neck pain that is mechanical in origin. However, different manipulative techniques

produce different results. The reasons for these differences are unclear. One of the reasons for the difference may be the size of the impulse used in the manipulation. If this was the case, manipulations of differing impulse sizes would produce different effects. This trial is designed to test the effect of two different types of neck manipulation on neck pain. The two manipulations are a high impulse manually applied manipulation (MAM) and a low impulse instrument applied manipulation (IAM).

The results of this research will be used by Lindsay Gorrell as part of her Masters of Research degree. The research has been initiated by Lindsay Gorrell and her supervisor, Dr Roger Engel from the Department of Chiropractic at Macquarie University. The project has been supported by the Higher Degree Research Fund at Macquarie University.

3 What does participation in this research involve?

In response to a public notice, volunteers will provide a medical history and undergo a physical examination of their neck that includes a series of non-invasive screening tests designed to detect risk factors associated with neck manipulation. After successfully completing the examination and screening stages and providing written consent, a volunteer will be enrolled as a participant in the trial. Each participant will then be assigned to one of three trial groups. Group A will receive a standardised active neck stretching program (S) designed to stretch the muscles in the neck. Group B will receive the same stretching program (S) plus one session of high impulse manually applied neck manipulation (MAM) administered to the lower neck. Group C will receive the same stretching program (S) plus one session of low impulse instrument applied neck manipulation (IAM) administered to the lower neck. A series of outcome measures will be taken before intervention (baseline) and immediately after intervention. These include: pressure pain intensity in the neck, global neck pain levels, neck range of motion, blood pressure, grip strength and skin temperature. Seven days after the intervention you will be asked via phone text message if you have any pain in your neck and if you do, how much. This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids researchers or participants jumping to conclusions.

There are no additional costs associated with participating in this research project, nor will you be paid. All SMT administered as part of this project will be provided to you free of charge. There will be no reimbursement for participation in this study. If you have a local Chiropractor, we encourage you to inform them of your participation in this project.

4 What do I have to do?

It is a requirement that for the duration of your involvement in the study you do not undergo any form of spinal manipulation as this could impact upon the results obtained. Other than this, you should continue with your normal routine/lifestyle.

5 Other relevant information about the research project

There will be approximately 63 participants in this study who will be divided into three equal groups.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Macquarie University.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment for mechanical neck pain. Other options are available; these include seeking treatment from another Chiropractor, visiting your GP or another health care practitioner. Your researcher will discuss these options with you before you decide whether or not to take part in this project.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research. However there is a growing body of evidence to show that spinal manipulative therapy is effective in the management of neck pain (3, 21, 24). It is expected that you will benefit from a reduction in both the level and intensity of your neck pain.

9 What are the possible risks and disadvantages of taking part?

Physical therapy treatments may cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with the researchers. The researchers will also be looking out for side effects. There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell them immediately about any new or unusual symptoms that you get. Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your researcher may need to stop your treatment. They will discuss the best way of managing any side effects with you.

Side Effect	How often is it likely to occur?	How severe might it be?	How long might it last?
Muscle soreness in neck	Possible	Mild	1-2 days
Neck stiffness	Possible	Mild	1-2 days
Pins & needles/numbness in arm	Rare	Mild/Moderate	1 week-1 month
Bone fracture (neck)	1 in 40,000	Moderate/severe	1-3 months
Stroke and/or death	1 in 5,000 to 1 in 10 million	Very severe	Permanent

Should participation in this research uncover a medical condition of which you were unaware, you will be immediately referred to a medical doctor. This discovery may or may not influence participation in the research project. This will be decided on a case-by-case basis by the primary investigator.

The effects of SMT on the unborn child are not known. Because of this, it is important that research project participants are not pregnant during the project. If you suspect you are pregnant you should advise your researcher immediately. You will be withdrawn from the research project.

If you become upset or distressed as a result of your participation in the research, the researcher will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be accessed through the Macquarie University Student Wellbeing framework and will be free of charge.

10 What will happen to my test samples?

There will be no collection of test samples from participants. Information which is collected during the research project may be subject to inspection (for the purpose of verifying the

procedures and data) by the relevant authorities and authorised representatives of Macquarie University. Your confidentiality will be maintained in the event of any inspection of research data.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your researcher will tell you about it and discuss with you whether you want to continue in the research project.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project it is required that you do not undergo SMT to any part of your spine. It is important to tell your researcher about any treatments you have received or changes to medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. If you do withdraw your consent during the research project, the researchers will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

Although unlikely, it is possible that this research project may be stopped unexpectedly. This may include reasons such as:

• Unacceptable side effects

• The treatment being shown to work and not need further testing.

15 What happens when the research project ends?

When the project ends your individual results and the de-identified group results can be made available to you on request. They will be sent to your nominated email address. The results will also be published in peer reviewed scientific journals and presented at scientific conferences.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

All named researchers will have the authority to access the information. Hard-copy and electronic information will be securely stored within the primary investigator's university office at Macquarie University. Participant identification numbers will be used for all collected data. If a participant needs to be re-identified their trial-specific identification number can be cross-checked against the master list. All data will be stored for a minimum of 15 years after the most recent publication. After this period, the information will be disposed of following standard procedures at Macquarie University for the destruction of confidential information. Participants may request their individual results and de-identified group results at completion of the trial. By signing the consent form you consent to the researchers collecting and using personal information about you for the research project. Your health records and any information obtained during the research project are subject to inspection (for the purpose of

verifying the procedures and the data) by the institution relevant to this Participant Information Sheet, Macquarie University, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above. The data collected in this project may be shared with other researchers working on other projects in the future. Any data supplied for this purpose will be in a non-identifiable format. In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment.

18 Who is organising and funding the research?

This research project is being conducted by Dr Roger Engel and Ms Lindsay Gorrell, a Masters of Research student. You will not benefit financially from your involvement in this research project. No member of the research team will receive a personal financial benefit from your involvement in this research project.

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Macquarie University. This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact Dr Roger Engel at roger.engel@mq.edu.au or telephone (02) 9850 6387.

Reviewing HREC name	Macquarie University HREC (Health)
HREC Executive Officer	Dr Karolyn White
Telephone	(02) 9850 7854
Email	Karolyn.White@mq.edu.au

Reviewing HREC approving this research and HREC Executive Officer details

Consent Form - *Adult providing own consent*

Title	The Effect of Spinal Manipulative Therapy on Mechanical Neck Pain
Short Title	SMT and Mechanical Neck Pain
Protocol Number	1
Project Sponsor	Macquarie University Department of Chiropractic
Principal Investigator	Dr Roger Engel
Associate Investigator(s)	Lindsay Gorrell
Location	Department of Chiropractic Outpatient Clinic 3 Innovation Rd, Macquarie University, 2109

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand. I understand the purposes, procedures and risks of the research described in the project.I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Macquarie University concerning my health and treatment for the purposes of this project. I understand that such information will remain confidential. I have had an opportunity to ask questions and I am satisfied with the answers I have received.I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care. I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Appendix E

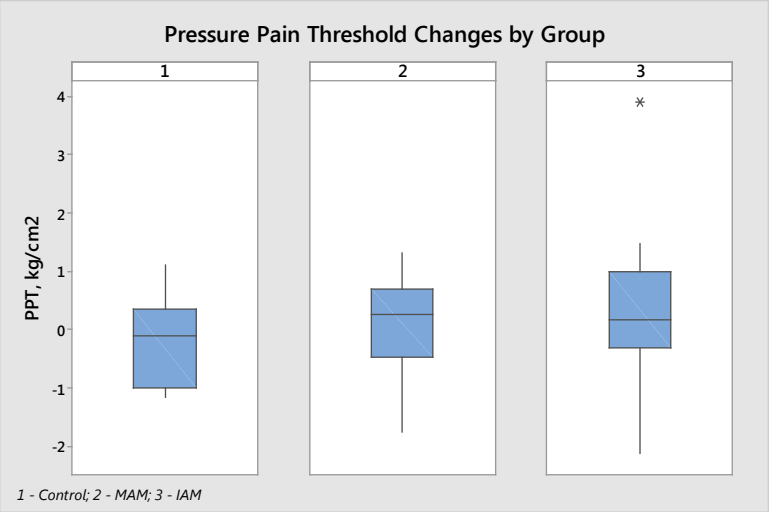

Figure 14 – Pressure pain threshold changes by group

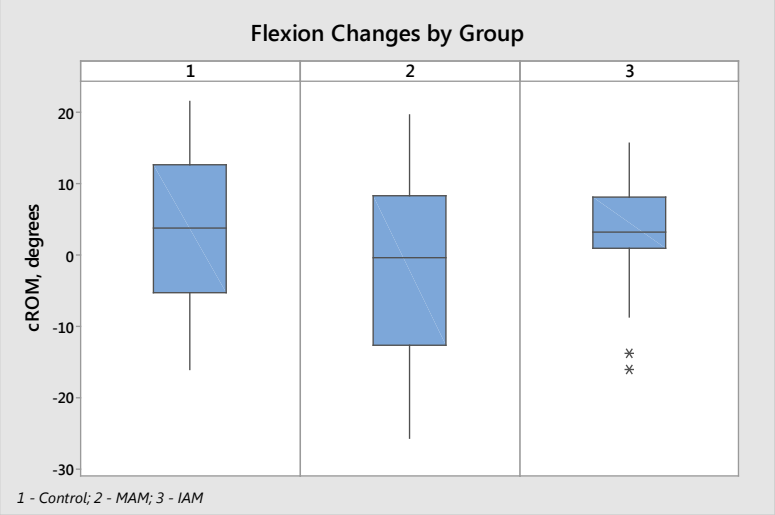

Figure 15 – Flexion changes by group

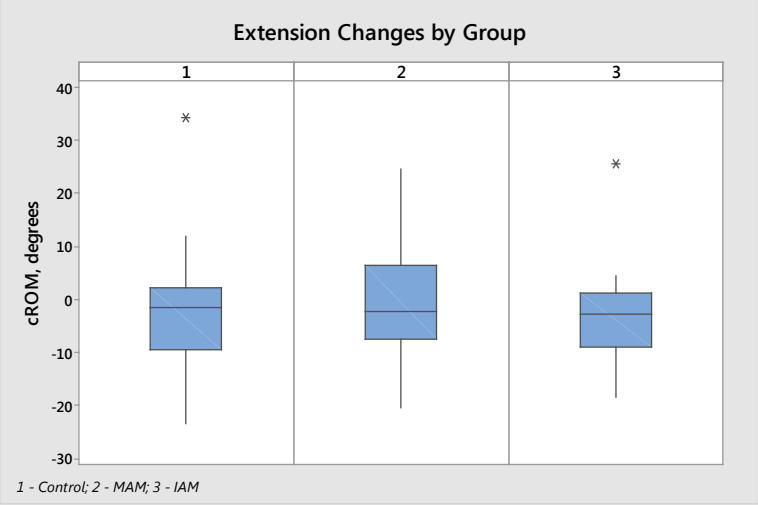

Figure 16 – Extension changes by group

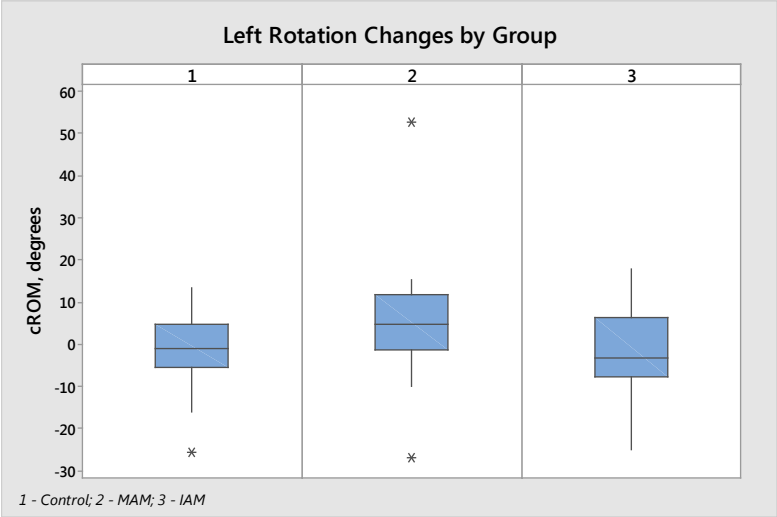

Figure 17 – Left rotation changes by group

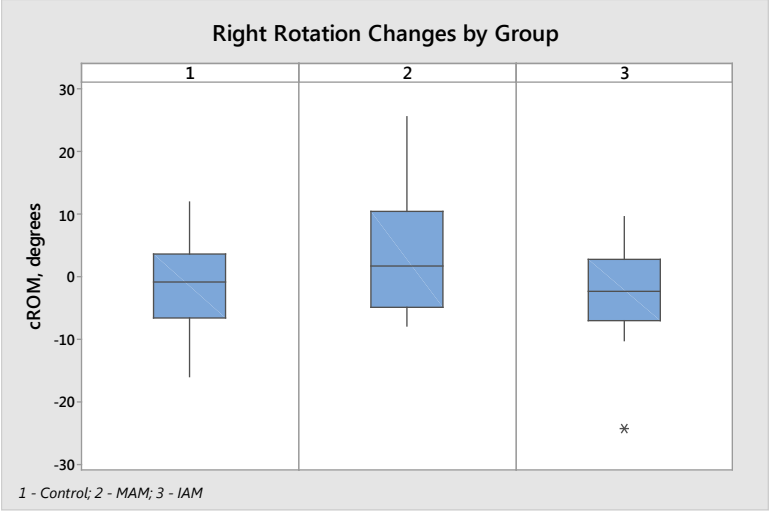

Figure 18 – Right rotation changes by group

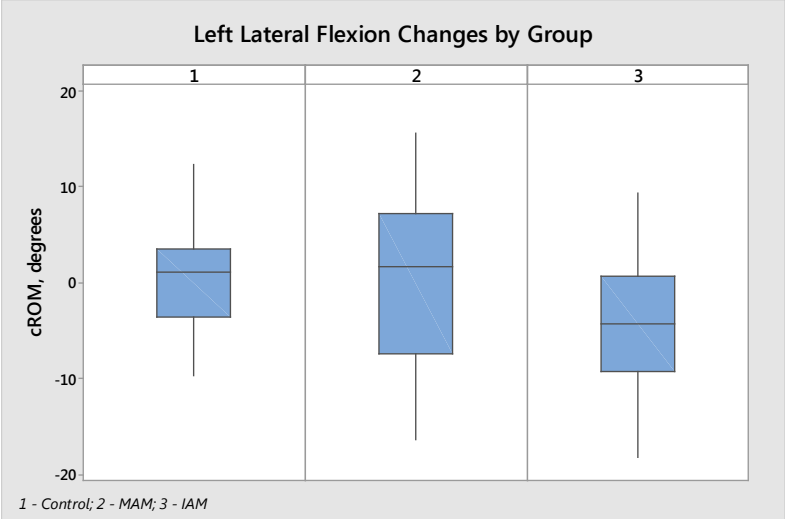

Figure 19 – Left lateral flexion changes by group

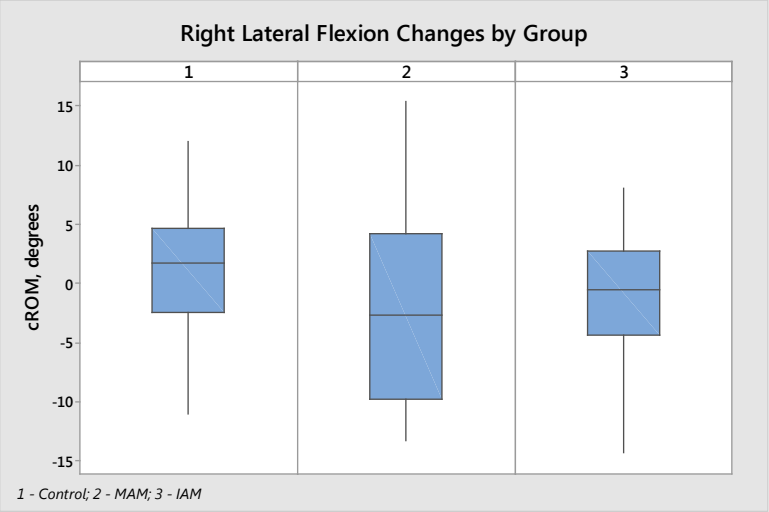

Figure 20 – Right lateral flexion changes by group

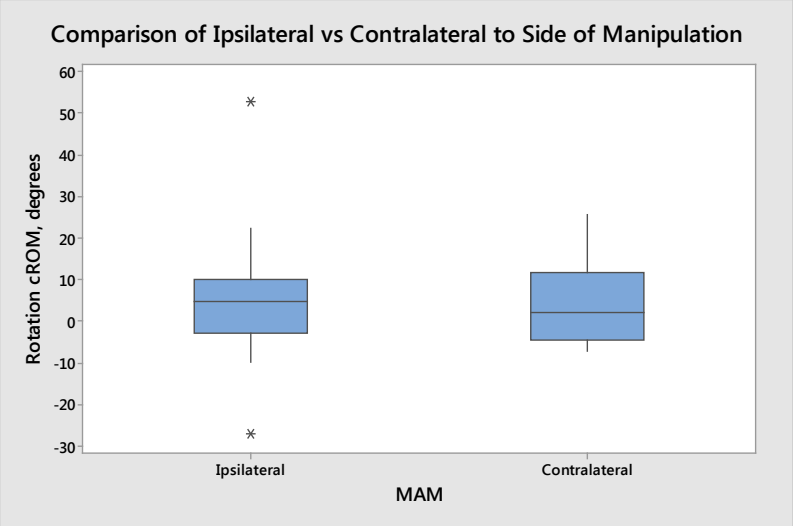

Figure 21 – MAM rotation changes ipsilateral *vs* contralateral to side of manipulation

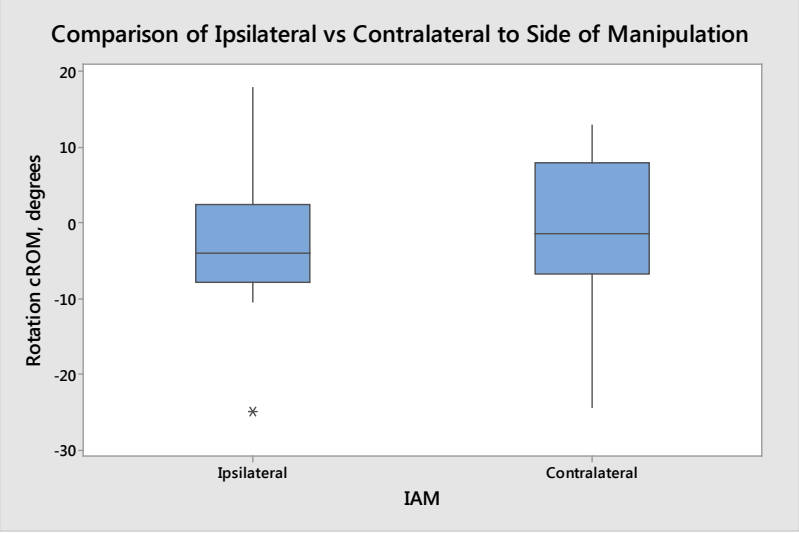

Figure 22 – IAM rotation changes ipsilateral *vs* contralateral to side of manipulation

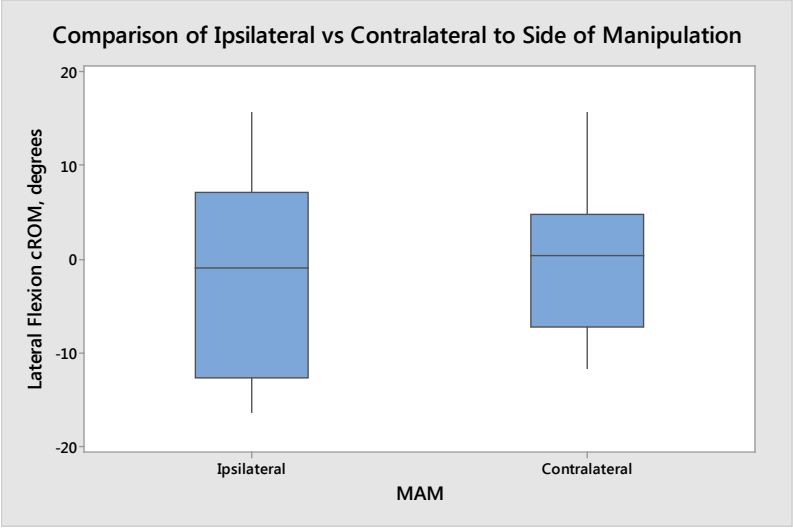

Figure 23 – MAM lateral flexion changes ipsilateral *vs* contralateral to side of manipulation

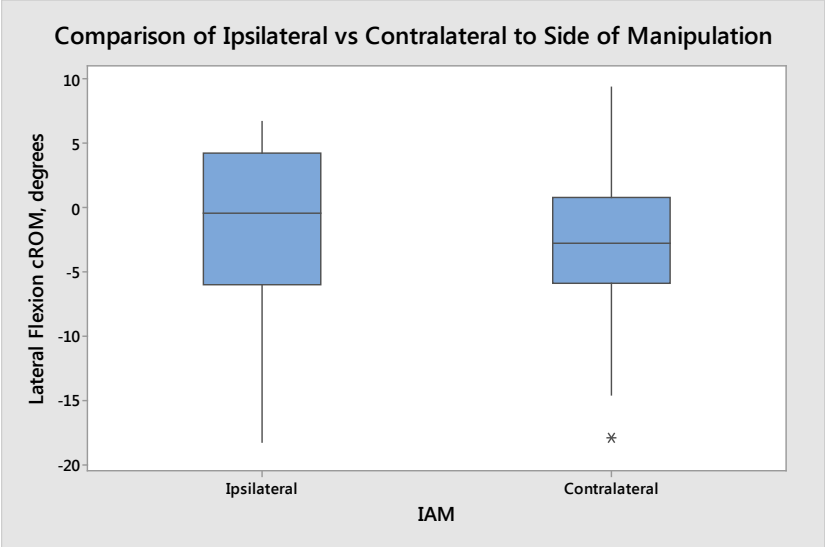

Figure 24 – IAM lateral flexion changes ipsilateral *vs* contralateral to side of manipulation

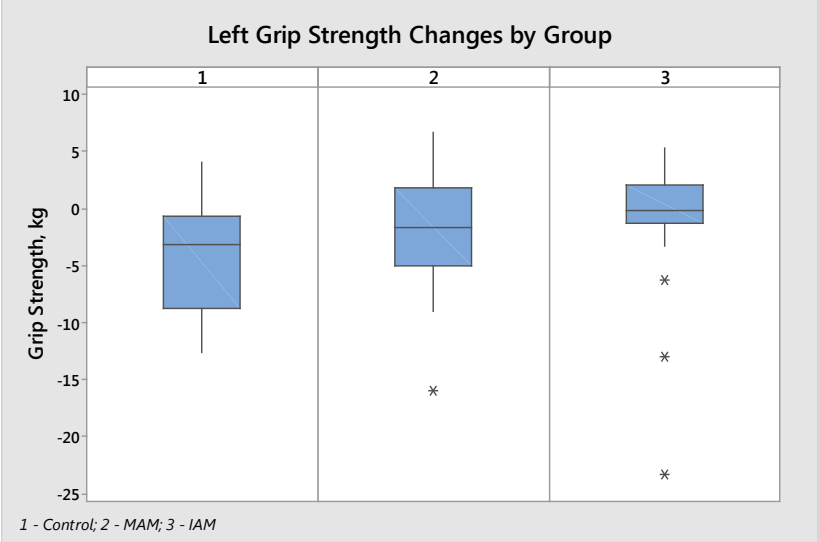

Figure 25 – Left grip strength changes by group

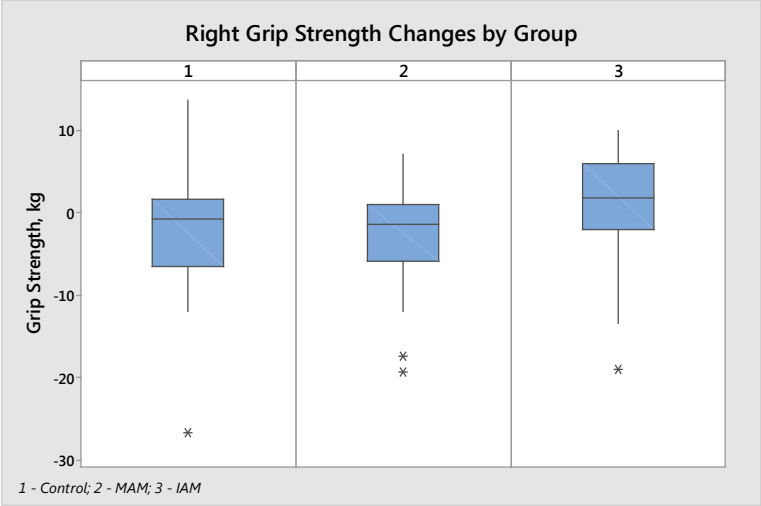

Figure 26 – Right grip strength changes by group

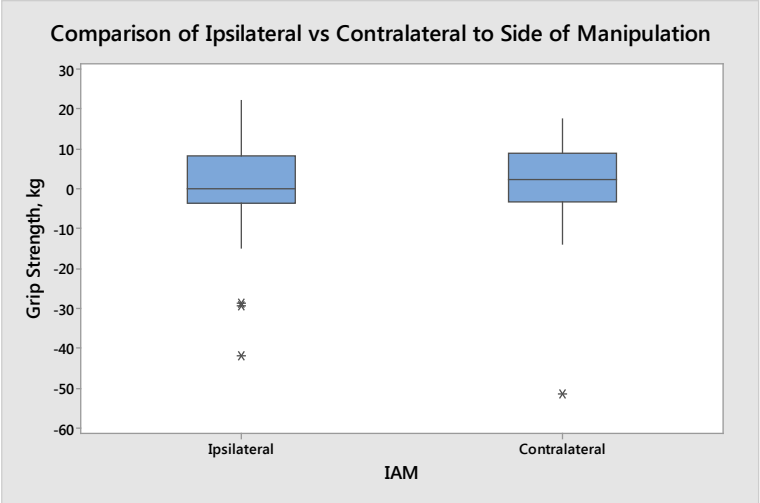

Figure 27 – IAM grip strength changes ipsilateral *vs* contralateral to side of manipulation

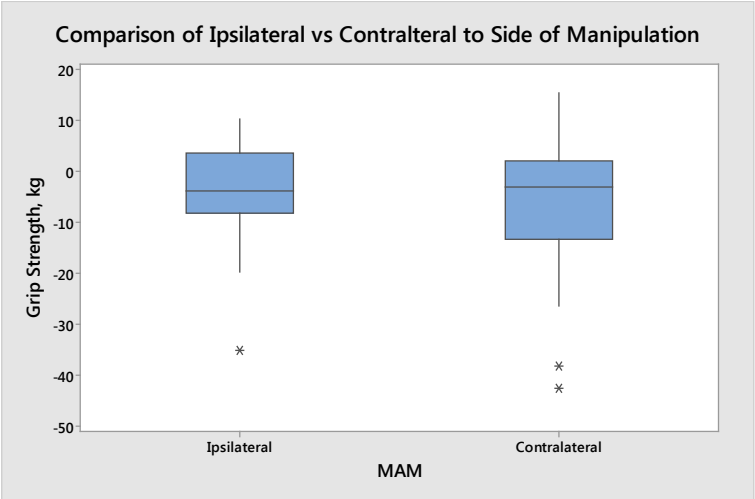

Figure 28 – MAM grip strength changes ipsilateral *vs* contralateral to side of manipulation

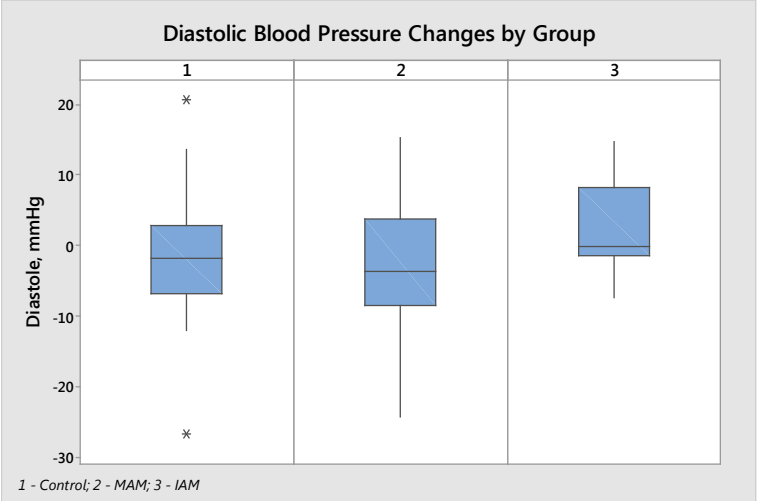

Figure 29 – Diastolic blood pressure changes by group

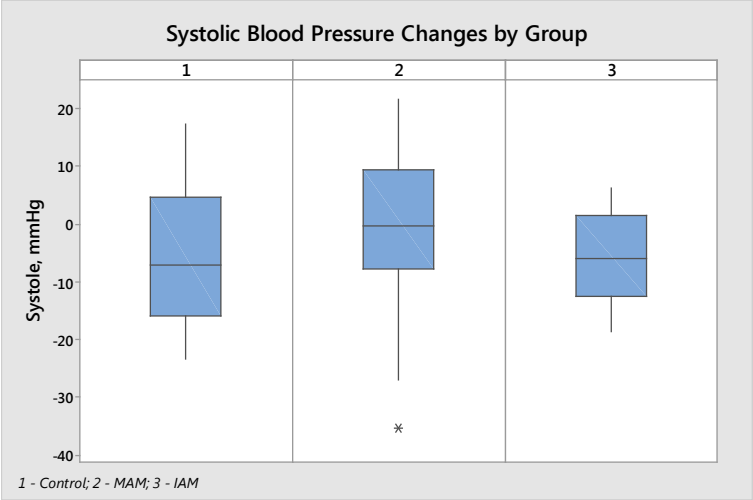

Figure 30–Systolic blood pressure changes by group